THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

A phase 1b study of neratinib, pertuzumab and trastuzumab with taxol (3HT) in primary metastatic and locally advanced breast cancer, and phase II study of 3HT followed by AC in HER2 + primary IBC, and neratinib with taxol (NT) followed by AC in HR+ /HER2- primary IBC
2016-0537

Study Chair: Rachel Layman

_____ _____
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 learn if adding neratinib to either taxol (paclitaxel) or to the combination of pertuzumab, trastuzumab, and paclitaxel can help to control metastatic or locally advanced breast cancer when given before other standard chemotherapy (doxorubicin and/or cyclophosphamide) and surgery. Researchers also want to find the highest tolerable dose of neratinib that can be used in these study drug combinations. The safety of these drug combinations will also be studied.

Please note: If you take part in this study, you may be given either trastuzumab or a biosimilar of that drug (which means it is identical to the study drug). Everything stated in this document about trastuzumab also applies to its biosimilar, including information about FDA approval status, side effects, and cost.

This is an investigational study. Pertuzumab and trastuzumab are FDA approved and commercially available for the treatment of HER2-positive breast cancer.

Paclitaxel, doxorubicin, and cyclophosphamide are FDA approved and commercially available for the treatment of breast cancer. Neratinib is FDA approved and commercially available. The drug combinations are investigational and are currently being used for research purposes only.

The study doctor can describe how the study drugs are designed to work.

The study drugs may help to control the disease. Future patients may benefit from what is learned. 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 hospitalization, a prolonged stay out of town, and/or because there are other standard options available.

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

You will receive up to 8 cycles of study drugs.

Neratinib, loperamide, and budesonide will be provided at no cost to you while you are on study. You and/or your insurance provider will be responsible for the costs of pertuzumab, trastuzumab, paclitaxel, doxorubicin, and/or cyclophosphamide, depending on which of these you receive.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive trastuzumab, pertuzumab, and/or chemotherapy which contains taxane (paclitaxel or docetaxel) or anthracycline (doxorubicin or epirubicin) and cyclophosphamide before surgery without taking part in this study. The study doctor will discuss the risks and benefits of these treatments with you. You may choose to receive other investigational therapy, if available. 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. The following screening tests will help the doctor decide if you are eligible:

- You will have a physical exam.
- Pictures of both breasts will be taken. Your private areas will be covered (as much as possible), and a picture of your face will not be taken unless there are lesions on your face.
- Blood (about 2 tablespoons) will be drawn for routine testing. Part of this blood draw will be used for a pregnancy test if you are able to become pregnant. To

take part in this study, you must not be pregnant. Urine may also be collected for the pregnancy test.
- You will have an EKG and either a MUGA scan or echocardiogram (ECHO) to check your heart function.
- You will have a chest x-ray, bone scan, mammogram, ultrasound, PET/CT scans or chest & abdominal CT scans, and/or MRIs performed to check the status of the disease.
- Blood (about 3 teaspoons) will be collected for research purposes, including genetic research.
- You will have a breast core biopsy to collect tumor samples for biomarker testing. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug. To perform a core biopsy, a sample of tissue is removed using a hollow core needle that has a cutting edge. A numbing drug will be given through a needle under the skin before the core biopsy. If you are taking part in both the IBC registry study (MD Anderson study 2006-1072) and this study, a core biopsy will be performed and samples will be collected separately for both studies in one setting.
- If it is available, tissue leftover from a previous procedure will be collected for biomarker testing.

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 treatment 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 1 of 3 study groups based on your screening results:

- If you are in Group A or B, you will receive neratinib, paclitaxel, pertuzumab, and trastuzumab. The difference between these 2 groups is that the dose of neratinib and paclitaxel may be different for participants in Group A, but all participants in Group B will receive the same dose.
    - If you are in Group A, you will be assigned to a dose level of neratinib based on when you join this study. Up to 5 dose levels of neratinib will be tested. Up to 20 total participants will be enrolled in Group A. 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. This will continue until the highest tolerable dose of neratinib is found. You will receive 4 cycles of the study treatment. At the completion of the 4th cycle, depending on your response, your doctor may decide to continue up to 4 additional cycles of the study therapy or start another treatment.
- If you are in Group B, you will receive doxorubicin and cyclophosphamide after receiving 4 cycles of the drugs listed above.
- If you are in Group C, you will receive neratinib and paclitaxel followed by doxorubicin and cyclophosphamide.

Up to 99 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration

All participants will take neratinib 1 time a day by mouth for the first week as a 1-week "pre-cycle". After that, the study cycle will be 21 days long in Cycles 1-4 and then either 14 or 21 days long in Cycles 5-8. Your drug administration schedule will depend on what group you are in. The study doctor will tell you what schedule you will follow.

If you are in Group A,

- You will take neratinib tablets 1 time a day by mouth with food at the same time each day (in the morning, if possible) during Cycles 1-4 (or up to 8 cycles). The study doctor will tell you how many tablets you need to take every day.
- You will receive paclitaxel by vein over about 1-3 hours on Days 1, 8, and 15 of Cycles 1-4 (or up to 8 cycles).
- You will receive pertuzumab by vein over about 1 hour on Day 1 of Cycles 1-4.
- You will receive trastuzumab by vein over about 1-2 hours on Day 1 of Cycles 1-4 (or up to 8 cycles).

If you are in Group B,

- You will take neratinib tablets 1 time a day by mouth with food at the same time each day (in the morning, if possible) during Cycles 1 - 4. The study doctor will tell you how many tablets you need to take every day.
- You will receive paclitaxel by vein over about 1-3 hours on Days 1, 8, and 15 of Cycles 1-4.
- You will receive pertuzumab by vein over about 1 hour on Day 1 of Cycles 1-4.
- You will receive trastuzumab by vein over about 1-2 hours on Day 1 of Cycles 1-4.
- You will receive standard-of-care doxorubicin and cyclophosphamide by vein over about 90 minutes on Day 1 of Cycles 5 - 8.

If you are in Group C,

- You will take neratinib tablets 1 time a day by mouth with food at the same time each day (in the morning, if possible) during Cycles 1 - 4. The study doctor will tell you how many tablets you need to take every day.
- You will receive paclitaxel by vein over about 1 - 3 hours on Days 1, 8, and 15 of Cycles 1 - 4.
- You will receive standard-of-care doxorubicin and cyclophosphamide by vein over about 90 minutes on Day 1 of Cycles 5 - 8.

If you are in Group B or C, you will have standard-of-care surgery after you finish receiving doxorubicin and cyclophosphamide. You will receive a separate consent form for the surgery that describes the procedure and its risks.

You will have a medication diary to record the information about taking neratunib, bring this diary and the medication bottles with the leftover drug to the clinic at the beginning of each cycles.

You will no longer be able to take the study drugs if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

Your participation on the study will be over after the follow-up period.

Study Visits

Before you receive study drug, at the end of the "pre-cycle", and then after Cycle 4, blood (about 3 teaspoons) will be drawn for research purposes, including genetic research.

***If you are in Group A*:**

- Before Day 1 of Cycle 1, you will have a breast core biopsy to collect tissue for biomarker testing.
- Blood (about 3 teaspoons) will be collected for research purposes, including genetic research.
- Before Day 1 of each cycle, and then before you begin the next treatment, you will have a physical exam.
- Before Day 1 of Cycle 1 and then before you begin the next treatment after Cycle 4, the study doctor will take pictures of both of your breasts.
- On Days 1, 8, and 15 of each cycle and before you begin the next treatment after Cycle 4, blood (about 1-3 tablespoon) will be drawn for routine tests.
- Before Day 1 of Cycle 1, and then before you begin the next treatment after Cycle 4, you will have a mammogram of the involved breast and an ultrasound of the involved breast and lymph nodes, or breast MRI if the doctor thinks it is needed.
- You will have a CT scan or PET CT scan or bone scan or chest X-ray after every 3 cycles if your doctor think it needed
- After Cycle 4, you will have a MUGA scan or echocardiogram (ECHO) to check your heart function.
- After Cycle 4 and you still have breast tumor, you will have another biopsy to collect tissue for biomarker testing.

***If you are in Group B or C*:**

- Before Day 1 of Cycle 1, you will have a breast core biopsy to collect tissue for biomarker testing and genetic research (for Group C only).
- Blood (about 3 teaspoons) will be collected for research purposes, including genetic research.
- Before Day 1 of each cycle and before surgery, you will have a physical exam .
- Before Cycle 1 and Cycle 5, and then before surgery, the study doctor will take pictures of both of your breasts.
- On the day of each cycle you are receiving chemotherapy and then before surgery, blood (about 1-3 tablespoon) will be drawn for routine tests.
- Before Day 1 of Cycle 1, before you begin receiving doxorubicin and cyclophosphamide, and then before surgery, you will have a mammogram of

the involved breast and an ultrasound of the involved breast and lymph nodes, or breast MRI if the doctor thinks it is needed.
- After Cycle 4, you will have a MUGA scan or echocardiogram (ECHO) to check your heart function. You may have a MUGA scan or ECHO every 3 months thereafter if the doctor thinks it is needed.
- During surgery, breast tissue samples will be collected to identify tumors for routine testing and for biomarker testing. No additional breast tissue will be removed in addition to what would already be removed during surgery.

Follow-Up

If you are in Group A:
- About 1 month after the last dose of study drug, you will be asked about your health and any side effects you may have had. You may be asked during a routine clinic visit or you may be called by a member of the study staff. If you are called, each call should last about 2 minutes.

If you are in Group B or C:
- About 1 month after surgery, you will be asked about your health and any side effects you may have had. You may be asked during a routine clinic visit or you may be called by a member of the study staff. If you are called, each call should last about 2 minutes.
- Then you will be followed every 6 months for 2 years for disease status. You may be asked during a routine clinic visit or you may be called by a member of the study staff. If you are called, each call should last about 2 minutes.

Other Information
While you are in this study:
- Follow the study visit schedule and instructions from the doctor and research staff. If you cannot come to a study visit, tell the study staff right away so the appointment can be rescheduled.
- It is important to report any issues such as side effects or other issues or questions you have.
- Please provide complete and accurate information to the best of your ability both for your safety and to make sure the study data is correct.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. These side effects will vary from person to person. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You should discuss these with the study doctor. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

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

Paclitaxel, pertuzumab, trastuzumab, doxorubicin, and cyclophosphamide each may cause low blood cell counts (red blood cells, platelets, and/or 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.

Neratinib Side Effects

Common (occurring in more than 20% of patients)

• fatigue • headache	• diarrhea	• nausea • abdominal pain

Occasional (occurring in 3-20% of patients)

• nail changes • skin rash • dry skin/itching • mouth blisters/sores (possible difficulty swallowing)	• loss of appetite • vomiting • dehydration • upset stomach • indigestion • weight loss	• urinary tract infection • abnormal liver tests (possible liver damage) • muscle spasms • nosebleed

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

• liver damage	• lung inflammation (possible difficulty breathing)

If you have severe diarrhea and/or vomiting, even for a short period of time, it is important that you tell the study doctor right away.

Paclitaxel Side Effects

Common (occurring in more than 20% of patients)

• abnormal EKG • swelling • flushing	• nausea/vomiting • diarrhea	• nerve damage (possible numbness,

• hair loss (partial or total) • mouth blisters/sores (possible difficulty swallowing)	• low blood cell counts (red/platelets/white) • abnormal liver tests (possible liver damage) • pain (muscle/joint)	pain, and/or loss of motor function) • abnormal kidney test (possible kidney damage) • allergic reaction • infection

Occasional (occurring in 3-20% of patients)

• low blood pressure (possible dizziness/ fainting) • slow heartbeat	• skin rash • abdominal pain • abnormal liver tests (possible yellowing of the skin and/or eyes)	• weakness • injection site reaction (possible redness, swelling, skin discoloration)

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

• fast/irregular heartbeat • blood clots in a vein (possible pain, swelling, and/or redness) • heart failure • abnormal EKG • heart attack • decreased blood supply to the heart • high blood pressure • fainting • decreased brain function (possible paralysis and/or coma) • decreased brain function due to liver damage • chills • seizure • severe sunburn-like rash at site of previous radiation (called radiation recall) • death of skin • inflammation at the site of previous tissue death	• worsening of existing scleroderma (severe hardened skin, which can cause difficult movement) • very severe blistering skin disease (with ulcers of the skin and digestive tract) • very severe blistering skin disease (loss of large portion of skin) • inflammation of the pancreas (possible abdominal pain) • inflammation of the intestines • dehydration • paralysis of the intestines • intestinal blockage • hole in the intestines (possible leaking contents into the abdomen) • decreased blood flow to part of the bowel	• difficulty walking • liver damage and/or failure • hearing loss • decreased kidney function • blockage in the lung (possible pain and/or shortness of breath) • lung inflammation and/or damage (possible difficulty breathing) • blood clots in the lung (possible failure to breathe) • lung damage (possible difficulty breathing) • difficulty breathing • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • tissue death at the injection site caused by drug leakage

	(possibly causing death of tissue)	

Pertuzumab Side Effects

Common (occurring in more than 20% of patients)

• fatigue • headache • skin rash • hair loss (partial or total) • nausea	• vomiting • mouth blisters/sores (possible difficulty swallowing) • loss of appetite	• constipation • diarrhea • low blood cells (white/red) • muscle pain/weakness

Occasional (occurring in 3-20% of patients)

• severe heart problems • swelling (arm/leg) • fever • nerve damage (possible numbness, pain, and/or loss of motor function) • difficulty sleeping • dizziness • itching • dry skin	• hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering) • nail changes • abnormal taste • loss of appetite • upset stomach • mouth/throat pain • abdominal pain	• abnormal liver tests (possible liver damage) • joint pain • teary eyes • nose bleed • difficulty breathing • cough • allergic reaction • infusion reaction (possible chills and/or hives)

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

• heart failure • low platelet cell count • build-up of fluid around the lungs	• severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

Frequency Unknown
Pertuzumab may cause the death of an unborn baby.

Trastuzumab Side Effects

Common (occurring in more than 20% of patients)

• severe heart problems • fever • chills • headache • nausea	• diarrhea • vomiting • abdominal pain • weakness • pain	• cough • difficulty breathing • infusion reactions (such as chills and fever)

		• infection

Occasional (occurring in 3-20% of patients)

• swelling (such as of the arm/leg) • heart failure • irregular heartbeat • fast heartbeat • high blood pressure • difficulty sleeping	• dizziness • depression • skin rash • loss of appetite • low blood cell counts (red and white) • muscle spasm	• abnormal sensation (such as pins and needles) • runny nose • sore throat • flu and/or flu-like symptoms • allergic reaction

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

• slow heartbeat • enlarged heart • heart attack • low blood pressure (possible dizziness/ fainting) • build-up of fluid in the tissue around the heart • shock caused by heart damage • spinal fluid build-up in the brain (possible headache, mental status changes, and/or coma) • swelling of the brain (possible headache and/or mental status changes) • mood disorder with extremes of happiness and sadness • stroke • coma • paralysis • fainting • seizure • shock • inflammation of nerves (possible pain and/or loss	• inflammation of the thyroid gland (possible tenderness in the neck) • high blood levels of calcium (possible altered mental status, weakness, and/or kidney damage) • vomiting of blood • intestinal blockage • bladder inflammation with or without bleeding(possible pain and/or urge to urinate) • inflammation of the pancreas (possible abdominal pain) • increased amount of blood • abnormal blood clotting • blood clot in a vein (possible pain, swelling, and/or redness) • low platelets counts • jaundice (yellowing of skin and/or eyes)	• back-up of urine into the kidney • kidney failure • difficulty breathing (possible due to narrowing of the airways) • lung inflammation and/or damage (possible difficulty breathing) • low oxygen level in the blood, which may be caused by anemia and/or lung infection (possible lightheadedness) • fluid in and/or around the lungs (possible difficulty breathing) • collapsed lung (possible difficulty breathing) • increased blood pressure in the lungs (possible difficulty breathing and/or heart failure) • life-threatening allergic reaction (such as difficulty breathing, low

of motor or sensory function) • nerve damage (loss of motor or sensory function) • underactive thyroid gland (possible weight gain, heart failure, and/or constipation)	• liver damage and/or failure • liver damage due to inflammation • difficulty walking • bone destruction • brittle/broken bones • deafness • decreased kidney function (possible kidney failure)	blood pressure, and/or organ failure) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • radiation injury

Trastuzumab may rarely cause you to develop another type of cancer (such as leukemia, a type of blood cancer).

Frequency Unknown

- birth defects that may lead to death of a newborn

<u>Doxorubicin Side Effects</u>

Common (occurring in more than 20% of patients)

- low white blood cell counts

It is not well known how often the following side effects of doxorubicin may occur:

• swelling • slow/extra/fast/irregular heartbeat • abnormal EKG • heart failure • enlarged heart • heart inflammation • inflammation of the tissue around the heart (possible chest pain) • severe heart problems • fatigue/lack of energy • skin rash • itching • skin sensitivity to sunlight or lamps	• hair loss (partial or total) • discoloration of sweat, urine, saliva, and/or tears • stopped menstrual cycle • dehydration • high blood levels of uric acid (possible painful joints and/or kidney failure) • abdominal pain • loss of appetite • diarrhea	• nausea • vomiting • death of colon tissue • stomach and/or small intestine ulcer • inability to have children • low blood counts (red/platelets) • weakness • difficulty breathing • injection site pain and/or inflammation • severe sunburn-like rash at site of previous radiation (called radiation recall)

	• mouth blisters/sores (possible difficulty swallowing)	

Serious side effects occurring in fewer than 1% of patients

• fever • coma • seizure • shock • very severe blistering skin disease (loss of large portion of skin) • very severe blistering skin disease (with ulcers of the skin and digestive tract)	• low sperm count • liver damage • abnormal liver tests (possible yellowing of the skin and/or eyes) • nerve damage (possible numbness, pain, and/or loss of motor function) • lung inflammation (possible difficulty breathing)	• allergic reaction, possibly life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure) • severe life-threatening infection (possible low blood pressure, kidney failure and/or heart failure)

Doxorubicin may cause you to develop another type of cancer (such as cancer of the bone marrow, and/or secondary acute myelogenous leukemia, a type of blood cancer).

<u>Cyclophosphamide Side Effects</u>

It is not known how often the following side effects may occur:

• hair loss (partial or total) • mouth blisters/sores (possible difficulty swallowing) • nausea • vomiting • abdominal pain	• loss of appetite • diarrhea • problems with production of sperm and eggs • inability to have children • stopped menstrual cycle	• low blood counts (red, platelet, white) • bladder inflammation and bleeding (possible pain and/or urge to urinate) • infection

Cyclophosphamide may cause you to develop another type of cancer (such as bladder cancer, acute leukemia [a type of blood cancer], lymphoma [a type of lymph node cancer], thyroid cancer, cancer of the bone marrow, and/or sarcoma [a type of cancer that can start in the soft tissue, bone, or other tissue].

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

• irregular heartbeat	• low blood levels of potassium (possible weakness)	• hearing loss

• build-up of fluid around the heart (possible heart failure) • inflammation of the heart and/or the tissue around the heart (possible chest pain and/or bleeding) • heart damage/failure, death of heart tissue, or other severe heart problems • 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) • brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss) • dizziness • very severe blistering skin disease (with ulcers of the skin and digestive tract) • severe sunburn-like rash at site of previous radiation (called radiation recall) • wound healing problems • very severe blistering skin disease (loss of large portion of skin)	• low blood levels of sodium (possible headache, confusion, seizures, and/or coma) • hormonal deficiency that affects the body's ability to control blood pressure and react to stress • decreased supply of blood to the abdomen • digestive system bleeding • enlarged bowel (possible abdominal pain) • inflammation of the intestines (possible bleeding) • inflammation of the pancreas (possible abdominal pain) • liver damage (possibly due to blood clots) • jaundice (yellowing of skin and/or eyes) • high blood levels of uric acid (possible painful joints and/or kidney failure) • ovarian scarring • urinary tract or bladder scarring • decreased testicle size and function • blood in the urine • blurry vision	• breakdown of muscle tissue (possible kidney failure) • death of kidney tissue (possible kidney failure) • difficulty breathing • lung inflammation (possible difficulty breathing) • problems with blood carrying oxygen (possible blue skin) • lung damage due to blood clots • increased blood pressure in the lungs (possible difficulty breathing and/or heart failure) • multiorgan failure • breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

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

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 **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.

Genetic research may result in the development of beneficial treatments, devices, new drugs, or patentable procedures. There are no plans to provide you compensation from such developments. The results of any genetic tests may be put in your health records. If this information were released, it could be misused. Such misuse could be distressing, and it could cause you or your family members to have difficulty obtaining insurance coverage and/or a job.
EKGs may cause discomfort while lying on the exam table, and the tape on the EKG pads may cause skin irritation.

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 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. 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.

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 can become pregnant or father a child, you must use appropriate birth control while on study and for 4 months after the last dose of study drugs. Appropriate, effective methods of birth control include:

1) Use of hormonal birth control methods: pills, shots/injections, implants (placed under the skin by a health care provider), or patches (placed on the skin);
2) Intrauterine devices (IUDs);
3) Using 2 barrier methods (each partner must use 1 barrier method) with a spermicide. Males must use a male condom (latex or other synthetic material) with spermicide. Females must choose either a diaphragm with spermicide, or cervical cap with spermicide, or a sponge (spermicide is already in the contraceptive sponge).
4) All male participants must agree and commit to use a barrier method of birth control while on treatment and for 4 months after the last dose of study drug

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 may result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1: If you agree, leftover blood and/or tissue samples collected from you while you are on study will be stored in a research bank at MD Anderson for use in future research related to cancer.

Before your samples can be used for research, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson. The IRB is a committee of doctors, researchers, and community members. The IRB is responsible for protecting study participants and making sure all research is safe and ethical.

Your samples will be given a code number. No identifying information will be directly linked to your samples. Only the researcher in charge of the bank will have access to the code numbers and be able to link the samples to you. This is to allow medical data related to the samples to be updated as needed.

There are no benefits to you for taking part in the optional procedure. You may stop taking part at any time. There will be no cost to you for taking part in the optional procedures.

Optional Procedure Risks:
MD Anderson and others can learn about cancer and other diseases from your **banked samples.** In the future, people who may do research with these samples may need to know more information about your health. This information may be collected from your medical record. MD Anderson will make reasonable efforts to preserve your privacy, but cannot guarantee complete privacy. Sometimes your samples may be used for genetic research about diseases that are passed on in families. **Genetic research** may result in the development of beneficial treatments, devices, new drugs, or patentable procedures. There are no plans to provide you compensation from such developments. The results of any genetic tests may be put in your health records. If this information were released, it could be misused. Such misuse could be distressing, and it could cause you or your family members to have difficulty obtaining insurance coverage and/or a job.

If you withdraw your consent to the storage of leftover samples in the tissue bank, then they will no longer be collected for storage. Any of your samples that remain in the tissue bank will no longer be used for research and will be destroyed.

However, if any of your de-identified samples were already released for research purposes before you withdrew consent, MD Anderson will not be able to destroy them.

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 leftover blood and/or tissue samples to be stored in a research bank at MD Anderson for use in future research related to cancer?

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 or Puma Biotechnology 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 may receive some reimbursement for costs that are a direct result of your participation, such as travel expenses. You will need to provide receipts for your expenses to be eligible for reimbursement. Please ask the study staff about this possible reimbursement.

Additional Information

4. You may ask the study chair (Dr. Rachel Layman, at 713-745-8401) 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. If you withdraw from this study, you can still choose to be treated at MD Anderson.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, Puma Biotechnology, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

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.

9. This study is sponsored and/or supported by: Puma Biotechnology.

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

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.

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 will 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. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you.

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.

Outside Care

Part of your care may be provided outside of MD Anderson by your home doctor(s).

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
   - Puma Biotechnology, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
   - Baylor College of Medicine (Bora Lim)
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

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

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

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

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol **2016-0537**.

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

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

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

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

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 (OTHER THAN TRANSLATOR, PARENT/GUARDIAN, OR STUDY CHAIR)	DATE

PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION