THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

A Phase I Study of the NovoTTF-100L(P)/ NovoTTF™-200T System to Enhance Antitumor Activity in Patients with Predominant Hepatic Metastatic Cancer
2014-0357

Study Chair: Siqing Fu

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 2 study drug combinations that can be given with either the NovoTTF™-100L(P) System or NovoTTF™-200T System at 150kHz.

The NovoTTF™-100L(P) and NovoTTF™-200T Systems are portable devices that use electrical fields intended to stop the growth of tumor cells by interrupting cancer cells' ability to divide. The NovoTTF™-200T is a successor to the previous version NovoTTF™-100L(P).

The first study drug combination is modified FOLFOX6 (leucovorin, fluorouracil, and oxaliplatin) mFOLFOX6 and bevacizumab. mFOLFOX6 plus bevacizumab is a standard-of-care option for colorectal cancer that has spread. Patients receiving this combination will also receive treatment with either the NovoTTF™-100L(P) or NovoTTF™-200T System. It is considered investigational to use mFOLFOX6 and bevacizumab in combination with the NovoTTF™-100L(P)/NovoTTF™-200T System.

The second study drug combination is liposomal doxorubicin, bevacizumab, and temsirolimus. Patients receiving this combination will also receive treatment with either the NovoTTF™-100L(P) or NovoTTF™-200T system. It is considered investigational to use liposomal doxorubicin, bevacizumab, and temsirolimus in combination with the NovoTTF™-100L(P)/NovoTTF™-200T System.

The safety of these combinations will also be studied. The study doctor can explain how the study drugs are designed to work.

This is an investigational study. The combination of mFOLFOX6 and bevacizumab is FDA approved and commercially available for the treatment of colorectal cancer. Doxorubicin is FDA approved and commercially available for the treatment of ovarian cancer. Bevacizumab is FDA approved and commercially available for the treatment of colorectal cancer. Temsirolimus is FDA approved and commercially available for the treatment of renal cell carcinoma. NovoTTF is an FDA-approved device to treat glioblastomas.

The use of the study drugs in combination with the NovoTTF system to treat cancer that has spread to the liver is investigational.

The combination of liposomal doxorubicin, bevacizumab, and temsirolimus is investigational and not approved for the treatment of any cancer type. The combination is currently being used for research purposes only.

While the device has not been proven effective in treating cancer that has spread to the liver, 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.

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

Your participation is completely voluntary. This is an experiment regimen and not standard of care. 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. You may not want to enroll in this study due to the potential for side effects, a prolonged stay out of town, or because you need to use the device for at least 18 hours a day. You may experience a delay or will not be able to receive the standard therapy due to potential side effects from the investigational part of the regimen.

This is the first time the NovoTTF™-100L(P) and NovoTTF™-200T systems have been used for this type of cancer.
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 doctor thinks it is in your best interest.

You and/or your insurance provider will be responsible for the cost of mFOLFOX6 and bevacizumab or liposomal doxorubicin, bevacizumab, and temsirolimus. You will receive NovoTTF at no cost to you.

You may choose not to take part in this study. You may choose to receive other chemotherapy or radiation therapy. You may be able to receive the study drug combinations without taking part in this study. You may choose to receive other investigational therapy, if available. The study doctor will discuss with you the possible risks and benefits of these treatments. 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.

1. STUDY DETAILS

Up to 55participants will be enrolled in this study. All will take part at MD Anderson.

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. If you have had some of these screening tests or procedures recently, they may not have to be repeated:

- You will have an electrocardiogram (EKG), echocardiogram (ECHO), or multiple gated acquisition scan (MUGA) to check your heart function.
- You will have a computed tomography (CT) scan or magnetic resonance imaging (MRI) to check the status of the disease.
- Blood (about 2 teaspoons) and urine will be collected for routine tests.
- You will have a tumor biopsy for biomarker testing. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug. The type of biopsy you have will depend on the type and location of the tumor.
- If you can 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 an arm based on the type of disease you have.

- If you are in Arm A, you will receive mFOLFOX6 and bevacizumab. You will also be treated with either the NovoTTF™-100L(P) or NovoTTF™-200T device based on when you join the study.

- If you are in Arm B, you will receive liposomal doxorubicin, bevacizumab, and temsirolimus. You will also be treated with either the NovoTTF™-100L(P) or NovoTTF™-200T device based on when you join the study.

Once you are assigned an arm, you will be assigned to a dose level of certain drugs based on when you join the study. Up to 6 participants will be enrolled at each dose level. The first group of

participants enrolled will receive a low dose level of the drug. You will be receiving a dose that is lower that what has been shown to be safe and effective. If no bad side effects are seen in this group, the next group will be treated with a higher dose level. This will continue until the highest tolerable dose level of the combination is found. Groups of participants in this part of the study are called "escalation" groups.

After the highest tolerable dose of Arm A and Arm B is found, additional participants with metastatic cancer of the liver will be enrolled at this level to further study the safety of this drug combination. This group is called the "expansion group."

The study doctor will tell you which Arm you are enrolled in, the dose of study drugs you will receive, and which NovoTTF system you will receive.

You will be trained in the use of the NovoTTF system by one of the following personnel: your doctor, study team, or a device technician trained by Novocure.

Study Drug Administration Each study cycle is 28 days.

If you are in Arm A:

- You will receive mFOLFOX6 by pump beginning on Day 1 of each cycle. This will be non-stop for 46 hours (about 2 days.)
- You will receive bevacizumab by vein for about 90 minutes on Day 1 and 15 of each cycle. If you are tolerating the infusion well, the next infusions may be reduced to 60 or 30 minutes.
- The NovoTTF™-100L(P) or NovoTTF™-200T system will be applied to your torso where the tumor is located for at least 18 hours a day. The study staff will show you how to do this.

If you are in Arm B:

- You will receive bevacizumab by vein for about 90 minutes on Days 1 and 15 of each cycle.
- You will receive liposomal doxorubicin by vein over 1-3 hours on Days 1 and 15 of each cycle. If you are tolerating the infusion well, the next infusions may be reduced to 60 or 30 minutes.
- You will receive temsirolimus by vein over 60-90 minutes on Days 1, 8, 15, and 22 of each cycle.

- The NovoTTF™-100L(P) or NovoTTF™-200T device system will be applied to your torso where the tumor is located for at least 18 hours a day. The study staff will show you how to do this.

Study Visits

During Weeks 1-4 of Cycle 1:

- Blood (about 2 teaspoons) will be drawn for routine tests.

During Week 1 of Cycles 2 and beyond:

- You will have a physical exam.
- Blood (about 2 teaspoons) will be drawn for routine tests.

During Week 2 of Cycles 2 and beyond, if you are in Arm B, blood (about 2 teaspoons) will be drawn for routine tests.

During Week 3 of Cycles 2 and beyond, blood (about 2 teaspoons) will be drawn for routine tests.

During Week 4 of Cycles 2 and beyond:

- Blood (about 1 teaspoons) will be drawn for biomarker testing.
- If you are in Arm B, blood (about 2 teaspoons) will be drawn for routine tests.

Every 2 cycles (or more often if your study doctor thinks it is in your best interest) you will have a CT, MRI, or PET scan to check the status of the disease.

You will no longer be able to take the study drugs if the disease gets worse, intolerable side effects occur, you develop new health problems, you become pregnant, or you do not follow the instructions on the study.

Your participation on the study will be over when you have completed the end-of-study visit.

End-of-Study Visit

About 30 days after the last dose of study drugs:

- You will have a physical exam.
- Blood (about 2 teaspoons) will be drawn for routine tests.
- Blood (about 1 teaspoons) will be drawn for biomarker testing.
- You will have a CT scan, MRI scan, or chest x-ray to check the status of the disease.

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 drugs/procedures.

NovoTTF™-100L(P)/ NovoTTF™-200T Systems Side Effects

The NovoTTF™-100L(P)/ NovoTTF™-200T Systems may cause redness or swelling of the skin, scaling, inflammation of hair follicles, mild pain and burning sensation, wound opening (less than 3 cm [about 1 inch]), wound drainage, ulcers on skin, complete wound dehiscence (complete opening of a wound), and/or deep cellulitis (an infection of the skin). If these side effects happen, they will be treated by the study doctor and should heal completely after use with the device is stopped.

NovoTTF™-100L(P)/ NovoTTF™-200T Systems are electrical devices. Potential risks of any electrical device include electrical or mechanical failure, electrical shock, and/or interference with other electrical devices. Novocure has taken appropriate actions to minimize how likely it is for these risks to happen.

Patients typically do not feel any 'electrical' sensation while receiving therapy.

Study Drug Side Effects

Fluorouracil, temsirolimus, liposomal doxorubicin, bevacizumab, and oxaliplatin each 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.

Fluorouracil Side Effects

It is not known how often the side effects of fluorouracil may occur.

chest pain due to heart trouble irregular heartbeat heart failure heart attack	headache stroke hair loss (partial or total) skin rash dry and/or peeling skin	mouth blisters/sores swollen throat loss of appetite diarrhea vomiting nausea
decreased blood supply to the heart blood vessel spasm (possible blockage of blood flow) darkened vein color blood clots in a vein (possible pain, swelling, and/or redness) abnormal brain function (affecting balance and coordination) confusion euphoria (unusual feelings of happiness or well-being)	skin sores hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering) syndrome skin sensitivity to sunlight or lamps very severe blistering skin disease (with ulcers of the skin and digestive tract) very severe blistering skin disease (loss of large portion of skin) nail loss	decreased supply of blood to the abdomen low blood cell counts (red, white, platelets) eye sensitivity to light vision problems eye twitching teary eyes (possibly due to narrowing of the tear duct) nosebleed life-threatening allergic reaction (such as difficulty breathing, low blood pressure, an/or organ failure)

Temsirolimus Side Effects

Common (occurring in more than 20% of patients)

swelling (arm/leg) pain fever skin rash high blood sugar (possible diabetes) low blood levels of potassium (possible weakness/muscle cramps)	low blood levels of phosphate (possible bone damage) high blood levels of fat (possible heart disease and/or stroke) mouth blisters/sores (possible difficulty swallowing) nausea loss of appetite diarrhea	abdominal pain low blood cell counts (red, white, platelets) abnormal liver test (possible liver damage) weakness abnormal kidney test (possible kidney damage) difficulty breathing cough infection

Occasional (occurring in 3-20% of patients)

chest pain headache difficulty sleeping itching	nail changes dry skin constipation abnormal taste	vomiting weight loss pain (back/joint) nosebleed sore throat

Exact frequency unknown but occurring in between 1 and 10 of patients:

high blood pressure blood clots in the veins (possibly in a deep vein and/or lung) chills depression acne	holes in the intestines (possible leaking contents into the abdomen) abnormal liver tests (possible yellowing of the skin and/or eyes)	muscle pain painful red eyes runny nose wound healing problems infusion reaction (possible chills and/or hives)

The intravenous (IV) infusion of temsirolimus may commonly cause you to have an allergic reaction and/or infusion reaction. These reactions include severe allergic reaction, breathing interruptions, chest pain, difficulty breathing, flushing, low blood pressure, and/or loss of consciousness. Life-threatening reactions, including fatal reactions, have occurred.

Rare but serious (occurring in fewer than 1% of patients)

build-up of fluid in the tissue around the heart seizure very severe blistering skin disease (with ulcers of the skin and digestive tract)	breakdown of muscle tissue (possible kidney failure) increased sensitivity to pain (possible burning, sweating, and/or swelling of the arms and legs) kidney failure	build-up of fluid around the lungs lung inflammation (possible difficulty breathing) fungal lung infection pneumonia drug leakage from injection site

Liposomal Doxorubicin Side Effects

Common (occurring in more than 20% of patients)

fever hand-foot syndrome (pain, swelling, blistering, and/or redness of the hands and/or feet)	skin rash nausea mouth blisters/sores (possible difficulty swallowing) vomiting	constipation diarrhea low blood cell counts (red, platelets, white) weakness pain (back)

Occasional (occurring in 3-20% of patients)

swelling (arm/leg) headache abnormal sensation (such as pins and needles)	dry skin hair loss (partial or total) loss of appetite upset stomach	intestinal blockage sore throat cough difficulty breathing

Liposomal doxorubicin may commonly cause infusion reactions such as allergic reactions. These reactions may be severe, and may include tightening of the airways, chest tightness, difficulty breathing, facial swelling, flushing, low blood pressure, chills, headache, herpes viral infection, shingles (painful skin rash), and/or itching.

Exact frequency unknown but occurring in 1-10% of patients

sudden stopping of the heart chest pain blood clots in a vein (possible pain, swelling, and/or redness) swelling low blood pressure (possible dizziness/ fainting) fast heartbeat flushing agitation anxiety chills confusion depression dizziness mood swings difficulty sleeping sleepiness acne sweating shedding and scaling of the skin (possible fatal loss of bodily fluids) itching change of skin color pale skin blistering skin rash dehydration high blood sugar (possible diabetes)	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) abdominal swelling loss of appetite fluid in the abdomen severe weight loss upset stomach difficulty swallowing throat inflammation gas gum disease swollen tongue paralysis of the intestines abnormal taste weight loss dry mouth bladder inflammation (possible pain and/or urge to urinate) difficult and/or painful urination white vaginal discharge pelvic pain frequent urination loss of bladder control urge to urinate uterine and/or vaginal bleeding	increased risk of bleeding abnormal liver tests (possible liver damage or yellowing of the skin and/or eyes) pain (joint/muscle/nerve/ ear) muscle tightness inflammation of nerves (possible pain and/or loss of motor or sensory function) nerve damage (loss of motor or sensory function) painful red eyes dry eyes inflammation inside the eye abnormal kidney test (possible kidney damage) blood in the urine interrupted breathing nosebleed build-up of fluid around the lungs runny nose allergic reaction (such as a skin reaction, and possibly severe)
	destruction of red blood cells	

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

enlarged heart irregular heartbeat heart failure build-up of fluid in the tissue around the heart blood clots in an artery (possible organ damage such as stroke and/or heart attack) mental status change seizure paralysis (one side of the body) fainting red or purple spots on the skin painful skin bumps allergic skin reaction death of skin very severe blistering skin disease (with ulcers of the skin and digestive tract)	very severe blistering skin disease (loss of large portion of skin) diabetes blockage of the intestine or colon by stool change in urine color severe high blood sugar due to uncontrolled diabetes low blood sugar inflammation of the pancreas (possible abdominal pain) bleeding at the injection site liver failure liver damage due to inflammation enlarged liver and spleen jaundice (yellowing of skin and/or eyes)	abnormal liver or bone test abnormal vision blindness inflammation of an eye nerve kidney failure difficulty breathing due to narrowing of the airways lung inflammation (possible difficulty breathing) collapsed lung (possibly difficulty breathing) blood clots in the lung (possible failure to breathe) low body temperature severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

Liposomal doxorubicin may rarely cause you to develop another type of cancer (such as oral cancer or acute myeloid leukemia, a type of blood cancer).

Bevacizumab Side Effects

Common (occurring in more than 20% of patients)

high blood pressure blood clots in a vein (possible pain, swelling, and/or redness) pain nerve damage (loss of sensory function) headache	loss of appetite constipation diarrhea mouth blisters/sores (possible difficulty swallowing) digestive system bleeding upset stomach	failure of the ovaries to produce hormones, which may be permanent (possible stopped menstrual cycle) bleeding nosebleed
dizziness fatigue hair loss (partial or total) abdominal pain	vomiting abnormal taste	low white blood cell counts difficulty breathing weakness abnormal kidney test (possible kidney damage)

Occasional (occurring in 3-20% of patients)

blood clots in an artery (possible organ damage such as stroke and/or heart attack) low blood pressure (possible dizziness/fainting) heart failure fainting bleeding in the brain and/or spinal cord stroke difficulty walking dry skin skin sores opening of a wound	shedding and scaling of the skin (possible fatal loss of bodily fluids) change of skin color low blood levels of sodium (possible headache, confusion, seizures, and/or coma) dehydration gas dry mouth hole in the intestines (possibly leaking contents into the abdomen) bleeding gums	inflammation or paralysis of the intestines weight loss nausea uterine and/or vaginal bleeding low platelet cell counts pain (back/muscle) voice changes runny nose lung inflammation (possible difficulty breathing) infusion reaction (possible chills and/or hives)

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

severe heart problems heart attack chest pain due to heart trouble severe increase in blood pressure (possible stroke) brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss) decreased brain function due to high blood pressure	stomach and/or small intestine ulcer vein blockage in the abdomen hole in the gall bladder (possible abdominal pain, gall stones, nausea, and/or infection) hole in the bladder destruction of red blood cells low red blood cell counts	deafness kidney failure decreased kidney function (possible kidney failure) coughing up blood increased blood pressure in the lungs (possible difficulty breathing and/or heart failure) blockage in the lung (possible pain, shortness of breath,
decreased blood flow to part of the bowel (possibly causing death of tissue) bleeding around the brain temporary stroke symptoms intestinal blockage	bone destruction (including destruction of the jaw bone) inflammation inside the eye blurry vision increased pressure in the eye (possible pain and/or blurry vision) detached retina (possible partial blindness)	and/or failure to breathe) abnormal hole inside the nose life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) wound healing problems

Bevacizumab may rarely cause an abnormal opening that develops between one area of the body and another (for example, an abnormal connection and opening in one or more places between the trachea [breathing tube] and esophagus, which may interfere with swallowing, digestion, and/or choking). This may result in death.

Rarely (in about 1-2% of patients), bevacizumab may cause bleeding in the brain in patients who have received bevacizumab for the treatment of primary brain tumors. You will be monitored for this complication and removed from the study if this were to occur.

If you are taking Coumadin (warfarin) or other blood-thinning drugs, you may be at higher risk of blood clots and/or bleeding.

Oxaliplatin Side Effects

Common (occurring in more than 20% of patients)

fatigue fever nausea diarrhea	vomiting abdominal pain constipation low blood cell counts (red, platelets)	abnormal liver test (possible liver damage) nerve damage (possible numbness, pain, and/or loss of motor function)

Occasional (occurring in 3-20% of patients)

swelling chest pain flushing pain headache difficulty sleeping dizziness	dehydration upset stomach abnormal taste gas low white blood cell counts	difficulty breathing cough runny nose injection site swelling, pain, and/or heat severe allergic reaction (possible hives, itching,
loss of appetite mouth blisters/sores skin rash hair loss (partial or total) low blood levels of potassium (possible weakness and/or muscle cramps)	abnormal liver tests (possible yellowing of the skin and/or eyes) joint and/or back pain shivering abnormal kidney test (possible kidney damage)	facial flushing, shortness of breath, difficulty breathing, sweating, low blood pressure)

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

brain damage that may be reversible (possible headache, confusion, seizures, and/or vision loss) blood clots tissue swelling hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering) low blood levels of magnesium (possible weakness and/or seizures) low blood levels of sodium (possible headache, confusion, seizures, swelling of the brain, and/or coma) abnormal blood acid/base balance (possible organ damage) paralysis of the intestines intestinal blockage inflammation of the pancreas (possible abdominal pain)	bleeding or blood in the stool blood in the urine liver damage possibly due to inflammation and/or blood clots increased risk of bleeding high blood pressure in a vein to the liver (possible liver damage) seizure difficulty walking inflammation of nerves (possible tingling, muscle twitching, drooping eyelid, difficulty forming or speaking words, muscle weakness, double vision, or seizures) loss of deep tendon reflexes (possible weakness) breakdown of muscle tissue (possible kidney failure)	inflammation of an eye nerve double vision kidney failure kidney inflammation (possible kidney damage/failure) death of kidney tissue (possible kidney failure) deafness type of pneumonia due to build-up of white blood cells (possible lung failure or death) abnormal sensation of the throat (possible difficulty breathing or swallowing) lung inflammation (possible difficulty breathing) low oxygen level in the blood (possible lightheadedness) drug leakage from the injection site (including death of tissues)

Do not take vitamin B6 (at doses higher than in a standard multivitamin tablet) if you are receiving oxaliplatin. B6 may make oxaliplatin less effective.

Leucovorin Side Effects

It is not known how often the side effects of leucovorin may occur.

skin rash itching skin redness	hives high blood platelet count (possible increased clotting) wheezing	allergic reaction, which may be life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure)

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.

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.

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.

A PET scan may cause you to 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 technicians will give comfort or the scanning will be stopped.

The PET scan exposes your body to radiation. The radioactive solution does not remain in your system for a long period of time. However, you should wait 2 hours before holding an infant or getting close to a pregnant woman to avoid exposing them to radiation. You should drink fluids after the scan to help remove the solution from your system.

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.

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

MUGA scans may cause allergic reactions to the radioactive tracer, injection site soreness, and/or swelling. They may cause damage to cells or tissue from being exposed to the radiation used in the scan. These side effects may occur in less than 10% of patients.

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 and will continue to be stored securely after the study.

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: You must use birth control during the study and for 30 days after the last dose of study drug if you are sexually active.

Examples of highly effective methods of birth control include:

- intrauterine device (IUD)
- birth control pills, injections, patches or implants

Examples of effective methods of birth control include:

- condom
- sponge
- diaphragm with spermicide
- cervical cap with or without spermicide

If you are a male who has had a vasectomy, you must use a barrier method of birth control (for example, condom with spermicide).

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: If you agree, leftover tumor tissue will be used for biomarker testing. If there is not leftover tissue, you will have a tumor biopsy. The type of biopsy you have will depend on the type and location of the tumor. The tissue will be banked at the ICT core laboratory at MD Anderson, and only the study staff and laboratory technicians will have access to the tissue. 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.

You do not have to agree to the optional procedure in order to take part in this study. 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 procedure.

Optional Procedure Risks:

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.

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES

Optional Procedure #1: Do you agree to allow leftover tissue samples or have a tumor biopsy to be used for biomarker testing?

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 Novocure for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-2933 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. Siqing Fu, at 713-792-4318) 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 will be removed from the study drug and will be asked to come to the clinic for safety tests. If you withdraw from this study, you can still choose to be treated at MD Anderson.

   If you stop being in the research, already collected data may not be removed from the study database. You may be asked whether the study doctor can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, Novocure, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson. Possible reasons for your removal without your consent include if the study doctor thinks it is in your best interest, if the disease gets worse, if study funding is stopped, if no supply of the study drug is insufficient, or if new information becomes available that might affect your participation.

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: Novocure.

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. The same level of data protection that covers your individual data does not apply to summary results (when data from the whole study is combined).

The Genetic Information Nondiscrimination Act (GINA) prohibits health insurers or health plan administrators from requesting or requiring genetic information of you or your family members, or using such information for decisions regarding your eligibility for insurance or your premiums. However, this law does not provide the same protection for disability, life insurance, or long-term care insurance. GINA also prohibits most employers (with 15 employees or more) from using genetic information when making decisions on your employment, including decisions related to hiring, firing, promotion, pay, and job assignments. Please contact the study doctor if you would like more information about GINA and how it protects you from genetic discrimination.

<u>Authorization for Use and Disclosure of Protected Health Information (PHI):</u>

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
- Novocure, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
- 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.

_____ Date/Time: _____

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.

_____ Date/Time: _____

ASSENT OF MINOR

ADULT ASSENT