Official Title:	**A Phase II Trial of Doxil, Carboplatin and Bevacizumab in Triple Negative Previously Untreated Metastatic Breast Cancer**
NCT number:	**NCT00608972**
Document Type:	**Study Consent - Main**
Date of the Document:	**10/07/2011**

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CONSENT TO TAKE PART IN A RESEARCH STUDY
Cancer Institute of New Jersey

Title of Study: A Phase II Trial of Doxil, Carboplatin and Bevacizumab in Triple Negative Previously Untreated Metastatic Breast Cancer

Principal Investigator: [redacted]

Introduction
This form is part of an informed consent process for a research study and it will give information that will help you to decide whether you wish to volunteer for this research study. It will help you to understand what the study is about and what will happen in the course of the study.

If you have questions at any time during the research study, you should feel free to ask them and should expect to be given answers that you completely understand.

After all of your questions have been answered, if you still wish to take part in the study, you will be asked to sign this informed consent form.

The study doctor (the principal investigator) or another member of the study team (an investigator) will also be asked to sign this informed consent. You will be given a copy of the signed consent form to keep.

You are not giving up any of your legal rights by volunteering for this research study or by signing this consent form.

Funding Company of Study
The doctor and/or Institution is the "Sponsor-investigator" of this Study. This means the doctor and/or Institution is the one who both initiates and actually conducts, alone or with others, a study, that is, under whose immediate direction the study drug is administered, dispensed, or used.

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A pharmaceutical company, [redacted] is a supporter of this research study. The study doctor is being paid to conduct this study according to a budget. The budget covers some of the costs of collecting the information, by the [redacted] esearch staff, required by the study. The drug bevacizumab will be supplied by [redacted] No other funding is provided by [redacted]

Why have I been asked to participate in this study?
You are being asked to take part in this study because you have metastatic (spread to other parts of the body) breast cancer. This type of cancer is usually treated with drugs called "chemotherapy" (drugs used to kill cancer cells). Your type of breast cancer is negative for a protein called HER2/neu. Your type of breast cancer is also negative for estrogen receptors (ER) and progesterone receptors (PR). HER2/neu, ER and PR are part of a family of receptors found on both cancer and normal cells. This family of receptors is important for cell growth and is found in many tumor types. The body is made up of tiny building blocks called cells that control every body function. Some cells stop working as they should and become cancerous cells. Unlike healthy cells, cancer cells grow and multiply abnormally, destroying body organs.

The purpose of this research study is to look at the effectiveness of a combination of doxil, carboplatin and bevacizumab on metastatic breast cancer.

This study is being conducted for the following research purposes:

- To find out what effects, if any, the study drug has on your cancer. For instance, will the study drug cause your tumor(s) to shrink or stop growing?
- To test the safety of the study drugs and to see what affects it has on you. For instance, are there any side effects? If so, what kind of side effects does the study drug cause? How severe are the side effects, and how often do they occur?
- To see if the study drugs have any effect on keeping your disease from getting worse.
- To monitor your health and overall well-being while taking the study drug.

Doxil is used in the treatment of solid tumors including breast cancer, bladder cancer, small cell lung cancer, thyroid cancer, gastric cancer, malignant lymphomas of both Hodgkin and non-Hodgkin type, and acute lymphocytic (lymphoblastic) leukemia.

If there is a shortage of doxil you will be able to receive treatment with epirubicin, a commercially available drug that is similar to doxil. Epirubicin has been approved by the FDA for the treatment of breast cancer. You will continue to have all other study treatments and safety monitoring as outlined in this consent.

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Bevacizumab is an antibody directed against vascular endothelial growth factor, or VEGF. VEGF is a potent, specific growth factor with a well-defined role in normal and abnormal blood vessel formation. It is present in a wide variety of normal tissues, but is produced in excess by most solid cancers (tumors). In the setting of cancer, VEGF promotes the growth of blood vessels that bring nutrients to tumor cells. In studies with laboratory animals, bevacizumab inhibits the growth of several different types of human cancer cells, including colon cancer cells, by blocking the effects of VEGF.

Bevacizumab received "accelerated" approval by the FDA for the treatment of metastatic breast cancer in 2008 based on positive early findings from a large clinical trial that bevacizumab in combination delayed the progression of breast cancer significantly longer than when chemotherapy was given alone. Final approval, however, was contingent on two additional studies in metastatic breast cancer demonstrating similar findings. Recent analysis of the two trials did not show the same benefit noted in the original study. Because of the potential side effects associated with the drug, and the less significant benefit noted in the two confirmatory studies, the FDA is considering withdrawing approval for the treatment in breast cancer. The FDA has encouraged, however, trials to determine populations of patients for whom the drug's benefits may exceed the risks. Triple negative breast cancer may be a subtype of breast cancer in which the benefits outweigh the risks. Therefore, we do not know how the information from the other studies applies to you with advanced triple negative breast cancer.

The FDA has approved carboplatin for use in treating ovarian cancer. Carboplatin is also used to treat various types of cancer. It is a chemotherapy drug that contains platinum. It is used alone or in combination with other medications to slow or stop cancer cell growth.

Who may or may not participate in this study?
In order to take part in this study, you must have the following conditions:

- You must be a woman with a diagnosis of metastatic breast cancer with none of the protein HER2/nue or estrogen receptors (ER) or progesterone receptors (PR) present.
- You must be ≥ 18 years old.
- You must not have received chemotherapy (drugs given to kill cancer cells) for metastatic breast cancer.
- Your cancer must be able to be measured, either by a physical examination or review of an x-ray.
- You cannot be pregnant or nursing a baby while on this study.
- If you are able to become pregnant and have a baby, you must have a pregnancy test that is negative (meaning you are not pregnant) and agree to use effective birth control, (e.g., abstinence, intrauterine device, oral contraceptives, barrier device with spermicide or surgical sterilization) during treatment and for three months after completing treatment.
- Your heart must be functioning normally. The study doctor will confirm this through standard tests used to measure heart function.

How long will the study take and how many patients will participate?
This study is estimated to enroll patients over two years. You will continue treatment until your disease worsens (progresses) or until you no longer are receiving benefit from the treatment. The study doctor

will decide if the treatment is no longer of benefit for you and if you should come off of the study.

About 50 patients total are expected to take part in this study. About 10 patients are expected to take part in this study at the [redacted]

What will I be asked to do if I participate in this research study?
Before you may take part in this study, you will need to answer questions and have the following tests and examinations to see if you are eligible. This is called screening. It is important that you answer all questions honestly and completely. If anything changes before or during the study, you must tell the study doctor. Based upon the answers to these questions and the results of the tests and examinations which have been performed there is a possibility that you may not qualify for participation in this study.

In some instances, certain tests or procedures conducted during the study may have to be repeated. For example, this can occur if some or all of the results are unusable. Also, you may be asked to have additional tests or examinations. For example, this can occur if an unexpected medical event occurs during the study. Before you begin treatment, you will need to have the following tests and procedures done:

- A history and physical exam.
- You will be asked about the extent of your physical activity and how you are generally feeling.
- Your weight and height will be taken.
- You will have blood drawn using a small needle or plastic tube, to check your blood cell counts, your blood chemistry, how your liver and kidneys are working and your electrolytes.
- You will have a urine test to monitor the level of protein in your urine.
- You will have an electrocardiogram done (also known as "ECG" or "EKG"). This is a painless paper tracing of your heart's normal electrical activity.
- You will have a special heart test called a MUGA scan. These tests will tell the doctors how well your heart works as a pump. This is important, since some of the drugs used in this study may affect your heart muscle. This test will be repeated several times during the study.

  A MUGA scan measures how well your heart pumps blood. During the MUGA scan, a radioactive marker is injected into a vein, and special equipment is used to measure the pumping capacity of your heart.

- If your doctor feels you need it, you may have to have a CAT scan or MRI (special tests which looks at the organs in your body).
- If you are able to become pregnant and have a baby, you must have a pregnancy test taken within one week of enrollment. The results of this test must be negative.

In addition during the study, you will have:

- Blood tests before treatment and weekly during the study. A complete blood count (CBC) will be checked weekly to make sure you have safe levels of the different types of blood cells in your body, and to see how the treatment effects a type of blood cell called the monocyte.

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- Other blood tests including chemistries and liver function tests will be done to check for side effects from the treatment. You will have a urine test before treatment to monitor the level of protein in your urine.
- A CAT scan (computed axial imaging) or an MRI (Magnetic Resonance Imaging) may be done every 8 weeks while you are on the study if the study doctor feels it is needed. The CAT scan or MRI will be done to look at the size and location (place) of tumors.
- You will also need to have an ECG (Electrocardiogram, also known as an "EKG" – a painless paper tracing of the heart's normal electrical activity).
- You will have a MUGA scan every 12 weeks and one month after your last treatment with the study drug combination.

The treatment schedule is as follows:
If you decide to take part in this study and are able to join based on the above criteria, you will have the following treatment.

You will have the chemotherapy (drugs used to kill cancer cells) with the drugs doxil, carboplatin and bevacizumab. A treatment period will be 28 days long. This period is known as a "cycle". All medications are given using a small needle or plastic tube into one of your veins.

Carboplatin and doxil will be given on Day 1 of each 28 day cycle.

Bevacizumab will be given on Day 1 after you have received carboplatin and doxil. Bevacizumab will also be given by itself on Day 15 of each 28 day cycle.

Days	1	2-14	15	16-28
carboplatin	X	No drugs given		No drugs given
doxil	X			
bevacizumab	X		X	

X = drug is taken

You will continue to receive these medications unless:
- You have severe, serious and/or excessive side effects.
- Your cancer becomes worse.
- You wish to stop taking part in this study.
- Your doctor feels it is not in your best interest to continue this treatment.

PLEASE NOTE: THERE IS NO PLACEBO (INACTIVE DRUG, OR "SUGAR" PILL) USED IN THIS STUDY. ALL PATIENTS WILL RECEIVE ACTUAL DRUG.

What are the risks and/or discomforts if I chose to participate in this study?
Any risks listed may be serious enough to result in hospitalization and/or death.

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The following are side effects, which may occur with the drug carboplatin:

Likely:

- Lowered number of red blood cells. Red blood cells carry oxygen to the organs in your body. A lowered number of red cells is known as anemia and can make you feel very tired and sometimes short of breath.
- Lowered number of white blood cells. White blood cells help to prevent infections. A lowered number of white blood cells may make it easier for you to get an infection.
- Lowered number of platelet cells. Platelet cells help your blood to clot. A lowered number of platelet cells may make it easier for you to bruise ("Black and blue" marks) or bleed.
- Nausea (a "sick" feeling in your stomach).
- Vomiting.
- Weakness
- A very tired feeling

Less Likely:

- Diarrhea.
- Constipation
- Hair loss, not only from your head, but also from your underarms, face, eyelashes and pubic area.
- You may not feel like eating.
- Numbness, tingling, and/or pain in your hands and feet. This is usually reversible.
- Changes in your levels of sodium (salt) and potassium in your blood.
- Mouth sores
- Yellowing of the eyes/skin
- Dark urine
- Changes in the amount of urine
- Pain/redness/swelling at the injection site
- Skin rash
- Itching
- Shortness of breath
- Wheezing
- Allergic reactions
- Hearing problems (e.g. ringing in the ears, hearing loss)

Rare:

- Mouth ulcers or blisters
- Blurred vision

The following are side effects, which may happen with the drug doxil:

Likely

- Nausea
- Vomiting

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- Asthenia (fatigue, weakness, tiredness)
- Anorexia (loss of appetite)
- Diarrhea
- Constipation
- Neutropenia (fever)
- Thrombocytopenia (abnormal drop in the number of blood cells involved in forming blood clots. These cells are called platelets)
- Anemia (below normal levels of red blood cells or hemoglobin, or both, which can be caused by many different conditions, including iron deficiency)
- Redness, pain, blistering of palms and soles of feet
- Hand-foot syndrome (HFS). It usually occurs on the palms of the hands and soles of the feet. It can also occur on other parts of the body where your clothes may be tight or where friction, pressure, rubbing, warmth, and/or sweating occur.
- Stomatitis, a mouth irritation characterized by inflammation or ulcers (sores). Some common symptoms of stomatitis include mouth sores, dry swollen tongue, dry cracked lips, pain or burning in the mouth, inability to eat or drink, or difficulty swallowing.

Less Likely

- Mild hair loss
- Flushing
- Chills and fever
- Irreversible weakening of the heart muscle (with higher doses) or heart problem such as heart failure or damage to the heart muscle

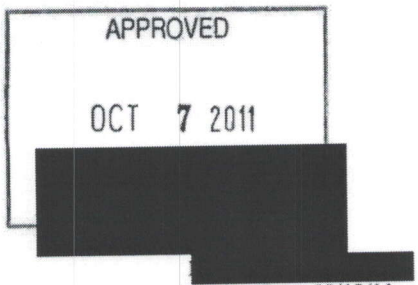
Rare but serious

- Shortness of breath
- Tightness of chest and throat
- Erythema multiforme: a rash consisting of welts, sometimes with purple or blistered areas in the center with itching, fever, general ill feeling
- Stevens-Johnson syndrome: potentially deadly skin disease resulting in facial swelling, tongue swelling, hives, skin pain, red or purple skin rash, blisters on the skin, mucous membranes (especially mouth, nose and eyes), shedding of the skin
- Toxic epidermal necrolysis: a life threatening skin disorder that causes blistering and peeling of the top layer of the skin

The following are side effects, which may happen with the drug Bevacizumab (Avastin®):

Likely:

- Diarrhea
- Nausea or the urge to vomit
- Vomiting
- Fatigue or tiredness



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- Headache or head pain
- High blood pressure

Less Likely:

- Lack of enough red blood cells (anemia)
- Fast heartbeat usually originating in an area located above the ventricles
- Feeling of spinning or whirling
- Belly pain
- Inflammation (swelling and redness) of the large bowel (colon)
- Constipation
- Heartburn
- Bleeding in some organ(s) of the digestive tract
- Partial or complete blockage of the small and/or large bowel. Ileus is a functional rather than actual blockage of the bowel.
- Irritation or sores in the lining of the mouth
- Reaction that can occur during or following infusion of the drug. The reaction may include fever, chills, rash, low blood pressure, and difficulty breathing.
- Chest pain not heart-related
- Pain
- Allergic reaction by your body to the drug product that can occur immediately or may be delayed. The reaction may include hives, low blood pressure, wheezing, swelling of the throat, and difficulty breathing.
- Infection
- Infection (collection of pus) around the rectum
- Premature opening of a wound along surgical stitches after surgery
- Increased blood level of a liver enzyme (ALT/SGPT)
- Increased blood level of a liver or bone enzyme (alkaline phosphatase)
- Increased blood level of a liver enzyme (AST/SGOT)
- Increased blood level of a liver pigment (bilirubin) often a sign of liver problems
- Increased blood level of a heart muscle protein (troponin I) indicating damage to the heart muscle
- Decreased number of a type of white blood cell (neutrophil/granulocyte)
- Weight loss
- Decrease in the total number of white blood cells (leukocytes)
- Loss of appetite
- Joint pain
- Abnormal changes in the growth plate that may affect the growth of long bones in very young children. This side effect appeared to be reversible after the treatment was stopped but has not been assessed with long-term use of the bevacizumab drug.
- Muscle pain
- Dizziness (or sensation of lightheadedness, unsteadiness, or giddiness)

- Fainting
- Sudden decrease of kidney function
- Blood in the urine
- More protein leaking into the urine than usual, often a sign of kidney disease
- Bleeding in the vagina
- Cough
- Shortness of breath
- Nose bleed
- Impaired wound healing
- Hoarseness
- Stuffy nose
- Itching
- Skin rash
- Hives
- Formation of a blood clot that plugs the blood vessel; blood clots may break loose and travel to another place, such as the lung

Rare but Serious:

- Damage of or clots in small blood vessels in the kidney that can cause complications, some of which are serious including abnormal destruction of red blood cells (hemolysis) or platelets (that help to clot blood) and kidney failure
- Collection of signs and symptoms that indicate sudden heart disease in which the heart does not get enough oxygen. Sudden symptoms such as chest pain, shortness of breath, or fainting could indicate heart disease and should be reported right away. Signs such as abnormal EKG and blood tests can confirm damage to the heart.
- Heart failure: inability of the heart to adequately pump blood to supply oxygen to the body
- Decrease in heart's ability to pump blood during the "active" phase of the heartbeat (systole)
- Heart attack caused by a blockage or decreased blood supply to the heart
- Irregular heartbeat resulting from an abnormality in the one of the lower chambers of the heart (ventricle)
- Ventricular fibrillation: irregular heartbeat that involves the lower chambers of the heart (ventricles) that results in uncoordinated contraction of the heart; life threatening and potentially fatal, needing immediate attention
- Gastrointestinal fistula: Abnormal hole between an organ of the digestive tract and another organ or tissue
- Gastrointestinal perforation : A tear or hole in the stomach or gut that can lead to serious complications and may require surgery to repair
- Sore (ulcer) somewhere in the digestive tract
- Serious, life-threatening allergic reaction requiring immediate medical treatment by your doctor. The reaction may include extremely low blood pressure, swelling of the throat, difficulty breathing, and loss of consciousness.
- Leakage from stomach due to breakdown of an anastomosis (surgical connection of two separate body structures)
- Bleeding in the brain

- Stroke caused by decreased blood flow to the brain
- Abnormal changes in the brain that can cause a collection of symptoms including headache, confusion, seizures, and vision loss associated with MRI imaging findings (RPLS)
- A condition in which the kidneys leak a large amount of protein into the urine that can cause complications including swelling and kidney failure
- Kidney failure
- Abnormal hole between part of the urinary system and another organ or tissue
- Abnormal hole between the vagina and another organ or tissue
- Abnormal hole between the lower breathing tube and the body cavity that surrounds the lungs
- Bleeding from the lungs
- Hole in the wall that separates the nostrils of the nose
- Abnormal hole between the breathing tube (windpipe) and the tube that goes from mouth to stomach through which food passes (esophagus). This is life-threatening and potentially fatal.
- Blockage or narrowing of a blood vessel (artery) that can cause damage or loss of function including a heart attack or stroke

The following are side effects, which may happen with the drug Epirubicin:

Likely:

- Reddish urine(for 1-2 days)
- Nausea
- Vomiting
- Mouth sores
- Dehydration
- Diarrhea
- Signs of congestive heart failure (e.g., shortness of breath, ankle swelling)
- Fever
- Signs of infection
- Pain, burning or stinging at the injection site
- Reversible alopecia (hair loss)
- Low blood cell counts (anemia, leukopenia, neutropenia, and thrombocytopenia)
- Fatigue
- Temporary or permanent loss of menstrual cycle in women
- Hot flashes
- Rash/itch

Rare but Serious:

Epirubicin causes several side effects, some of which can be severe. In some cases, epirubicin may need to be stopped because of these side effects.

One of the most dangerous side effects of epirubicin is heart damage. In its most severe form, this heart damage manifests as congestive heart failure, which can be fatal. Heart problems can occur months or years after stopping epirubicin. The probability of developing heart failure is dependent on the cumulative dose of epirubicin, which is the total amount of epirubicin given after all chemotherapy cycles are finished. The risk of congestive heart failure is very low, less than 1%, following a cumulative

dose of 550mg/m2 and less than 3% after a cumulative dose of 900 mg/m2. The risk of congestive heart failure is a condition where the heart does not pump enough blood to support the needs of the body.

Secondary Leukemia has also been reported within three years of stopping epirubicin. Based on several studies, the risk ofsecondary leukemia has been estimated at 2% after eight years. Secondary leukemia is a cancer of the white blood cells in your blood that fight infections that might be caused by treatment with epirubicin.

Other risks associated with the study:

- **In addition to the known side effects listed for three medicines used in this study, there is also the possibility of a new or unanticipated side effect when the three medicines are combined together**
- There is the risk that this treatment may not work for you.
- Side effects of having blood drawn from a vein or IV (intravenous) therapy: When your blood is drawn, there is a possibility that there may be a bruise ("black and blue" mark), bleeding or infection (rarely) at the place where the needle entered your vein.
- Some patients who have an MRI may develop claustrophobia. It is important to let your doctor know if you have this problem. If you have a pacemaker or other metal object or device in your body or have ever worked with sheet metal you may not be able to have an MRI.
- Some of the tests that will be performed on you (X-rays, CT scans, MRI, and/or bone scans, and MUGA scan [if required]) will expose you to controlled amounts of radiation. The CT and/or MRI scans and MUGA scan will involve dyes being injected into your vein. There is a risk of allergic reaction to the dye. The injection of substances such as dyes into your blood may cause pain, swelling, bruising, irritation or redness at the site, feel faint, or infection at the site of the needle puncture. The collection of tumor tissue adds no additional risk to you since this tumor tissue was obtained from a previous biopsy. It is important that you report any side effects to your study doctor as soon as possible. You should not wait until your next scheduled visit.

Other Medications or Supplements:

You should not take any over the counter medicines, herbal products, vitamins or food supplements or any other types of special products while participating in this study, unless you tell the study doctor and permission is given to continue taking these medicines. There could be drug interactions with the over the counter products, not known at this time, that could potentially harm you. You should also tell the study doctor about any and all medicines other doctors may have prescribed for you to take.

Pregnancy and Childbearing Precautions:

The drugs in this study may affect the way a woman's ovaries work and her ability to get pregnant. If you are a woman who is able to become pregnant and have a baby and are sexually active with men, you must agree to not become pregnant during the time you are taking part in this study because it is not known what effects this treatment may have on a developing baby. If you are not willing to use adequate birth control, you must not sign up for this study. Adequate birth control includes: abstinence, a diaphragm with cream to kill sperm cells, an intrauterine device ("IUD"), latex condoms, a tubal ligation (having your "tubes tied") or oral contraceptives. You should continue to use adequate birth

control measures for at least 3 months after study therapy.

You must not breast feed a baby while taking part in this study and for 3 months after stopping the study, because the effects of this treatment on a baby cannot be determined.

If you have any questions about birth control, please speak to your study doctor. If you become pregnant, you must immediately tell the study doctor, and you will stop study therapy.

Are there any benefits if I choose to participate in this research study?
The benefits of participating in this study may be that your cancer may shrink or stay the same size for a long period of time. However, you may receive no direct benefit from taking part in this study.

What are my alternatives if I don't want to participate in this study?
Your doctor is willing to discuss the benefits and side effects of other forms of treatments other than this study that are available. These include:

- Other usual chemotherapy for your type of cancer, which may include the same types of chemotherapy that is used on this study.
- Other experimental studies with chemotherapy, hormones, radiation therapy, or new anti-cancer agents may be available for your disease.
- You may also choose no further treatment, with care and medicines to help you feel more comfortable.

Please feel free to discuss these other options with your doctor and ask any questions you may have. Take as much time as you need to make your decision

How will I know if there is information learned that might affect my willingness to participate in this research study?
During the course of the study you will be updated about any new information that may affect your willingness to remain in the study. If new information is learned that may affect you after the study has completed, you will be contacted.

Who will have access to my research records from this study?
By taking part in this study, you should understand that we will be collecting your personal health information. This includes, but is not limited to, demographic data (your name, date of birth, etc.) and data on your health (your history, physical findings, laboratory results, study-related findings, etc.). During the course of this trial, study visitors (known as monitors) will review your medical and research record to make sure we collected your study information properly. These monitors are employed by The Cancer Institute of New Jersey. Sometimes, they will need to take notes or photocopy parts of your medical record. We will replace your name on these pages with your assigned study number. This data will be reported to other staff at The Cancer Institute of New Jersey on a regular basis, as required by the study. The Cancer Institute of New Jersey will analyze, process, and store your data with electronic data processing systems. The authorization for use of your research data has no expiration date. Your

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personal health information may be subject redisclosure by [redacted] Human Research Services and if it is redisclosed, it may no longer be protected. Your personal identity, however, that is your name, address and other identifiers will remain confidential (a study number will be used for your name). Only the study doctor, research team and study monitor will be able to link the study number to your name. Your data may also be forwarded to domestic and foreign drug regulatory agencies if you have an adverse (bad) reaction.

The following groups of people may also be allowed to inspect sections of your medical and research records related to this study:

- [redacted]

Your information may also be submitted to domestic (within the United States) and foreign drug regulatory agencies in applications for marketing authorization and may be used in scientific publications (journals, articles). If the findings from the study are published, you will not be identified by name. Your identity will remain confidential unless the law requires us to give out this information, such as in the case of reporting people who have diseases others can catch. In this case, you will be informed of the intent to disclose (give out) such information to the authorized state agency. Such a law has already existed in [redacted]

You have the right to look at your personal information at your study doctor's office and to request any corrections of your personal data that are wrong.

If you do not sign this approval form, you will not be able to take part in this research study.

Will there be any costs to me to participate in this study?
The drug Bevacizumab will be supplied at no cost to you by [redacted]

Your health insurance carrier or third party payer will be billed for the cost of routine blood tests, x-rays, scans and other routine tests that would be part of your standard medical care even if you were not taking part in this study. Whatever costs your insurance company does not pay will be your responsibility. All doctor's or hospital costs will be charged to you in the same way as if you were not part of this study.

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Will I be paid to participate in this study?
You will not be paid or receive any other form of compensation to take part in this study.

What will happen if I become injured during the study?
If you participate in this study, you will be exposed to certain risks of physical injury in addition to those connected with standard forms of therapy. Please refer to Risks/Discomforts section. Medical and/or dental treatment will be arranged by [redacted] for participants who sustain physical injuries or illnesses as a direct consequence of participation in this research. Your health insurance carrier or other third party payor will be billed for the cost of this treatment. No additional financial payment is available. You are not giving up any of your legal rights by signing this form or by participating in this research study.

[redacted] will not provide payment for any medical expenses, which you may incur as a result of your participation in this study.

What will happen if I do not wish to participate or decide not to continue in the study?
You may choose not to be in the study and if you do choose to participate it is voluntary. You may also refuse to participate, or change your mind at any time. If you do not want to enter the study or decide to withdraw (stop taking part) from the study, your relationship with the study staff will not change, and you may do so without penalty or loss of benefits to which you are otherwise entitled. If you do not want us to continue using the data we have already collected about you, you must withdraw your permission in writing to [redacted] Even if you withdraw our permission to use the data about you, we cannot retrieve (get back) any of the information previously submitted. We are required by the Food and Drug Administration however, to continue to report anything that relates to the safety of these drugs.

At any time, the study doctor can decide to withdraw you from this study because to take part further would not be in your best interest. Your study doctor can stop treatment even if you are willing to continue. If you, or your study doctor, decide to withdraw you from the study you may be asked to return for a final visit for safety reasons.

Also, you should understand that the study doctor can withdraw you from the study at any time if you do not follow the instructions related to the study, or if you need a different treatment.

Who may I contact if I have any questions?
If you have any questions about your participation in this study, you can contact the study doctor:

[redacted]

If you have any questions about your rights as a research subject, you can contact:

[redacted]

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ADDITIONAL RESEARCH TESTING, FUTURE USE TISSUE SAMPLES OR THE INTENT TO STORE SAMPLES:

Please initial each one of the following sentences that applies:

_____ I agree to be contacted by the Investigators for future research studies.

_____ I **do not** agree to be contacted by the Investigators for future research studies.

_____ I agree to the use of my blood/tissue for future research

_____ I **do not** agree to the use of my blood/tissue for future research

I understand that if I do not want my samples used for future research it will not affect my ability to take part in this study or in future studies.

What are my rights if I decide to participate in this research study?
You have the right to ask questions concerning any part of the study at any time. You should not sign this form unless you have had a chance to ask questions and receive answers to all of your questions.

I have read this entire form, or it has been read to me, and I believe that I understand what has been discussed. All of my questions regarding this form or this study have been answered. I agree to participate in this research study and have been given a copy of this consent.

Patient Name: _____

Patient Signature: _____ Date:_____

SIGNATURE OF READER/TRANSLATOR IF THE PATIENT DOES NOT READ ENGLISH
The person who has signed above, _____, does not read English well. I read English well and am fluent in _____, a language the patient understands well. I understand the content of this consent form and have translated for the patient the entire content of this form. To the best of my knowledge, the patient understands the content of this form and has had an opportunity to ask questions regarding the consent form and the study, and these questions have been answered.

APPROVAL EXPIRES
AUG 1 7 2012
[redacted]

APPROVED
OCT 7 2011
[redacted]

[redacted]

[redacted]

Reader/ Translator: Name: _____

Signature: _____ Date: _____

Witness: Name: _____

Signature: _____ Date: _____

SIGNATURE OF INVESTIGATOR OR RESPONSIBLE INDIVIDUAL

To the best of my ability, I have explained and discussed the full contents of the study including all of the information contained in this consent form. All questions of the patient have been accurately answered and the patient has been given a copy of the consent.

Name of Investigator/Person Obtaining Consent: _____

Signature: _____ Date: _____

APPROVAL EXPIRES
AUG 17 2012
INSTITU [redacted]

APPROVED
OCT 7 2011
[redacted]

[redacted]

[redacted]