

**MARQUETTE GENERAL HEALTH SYSTEM**

**Regional Medical Center**

**CONSENT TO PARTICIPATE IN AN INVESTIGATIONAL STUDY**

**TITLE: NSABP B44 – BETH (“Bevacizumab with Trastuzumab Adjuvant Therapy in HER2+ Breast Cancer”) A Multicenter Phase III Randomized Trial of Adjuvant Therapy for Patients with HER2-Positive Node-Positive or High Risk Node-Negative Breast Cancer Comparing Chemotherapy Plus Trastuzumab with Chemotherapy Plus Trastuzumab Plus Bevacizumab CIRG (TRIO) 011/NSABP B-44-I/BO20906**

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This is a clinical trial, which is a type of research study. You are being asked to take part in this study because you have "HER2-positive" invasive breast cancer. HER2-positive means that the cancer makes too much of a protein called HER2. Too much of this protein can cause normal cells to receive too many growth signals, which can turn a normal cell into a cancer cell and can change the way it responds to treatment. Your doctor has told you that chemotherapy and other therapy will decrease the chance of your cancer returning.

Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose voluntarily to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

**Who is conducting the study?**

Two research groups will be conducting the BETH Trial: the Cancer International Research Group (CIRG) and the National Surgical Adjuvant Breast and Bowel Project (NSABP). Marquette General Hospital is also conducting the trial locally.

**Why is this study being done?**

This study is being conducted for the following reasons:

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- The main purpose of this study is to learn if adding bevacizumab to standard treatment with chemotherapy and trastuzumab for HER2-positive breast cancer will prevent breast cancer from returning. Bevacizumab is called a targeted therapy because it works by targeting a protein called vascular endothelial growth factor (VEGF) which helps new blood vessels form. Without new blood vessels, the growth of the tumor is slowed. Previous studies with bevacizumab have produced promising results in patients with various types of cancer. Bevacizumab is considered investigational because it is still being researched and has not yet received approval from the U.S. Food and Drug Administration (FDA) for use in treating breast cancer.
  - Trastuzumab is also called a targeted therapy because it targets HER2-positive breast cancer cells. Trastuzumab blocks the HER2 protein on the surface of the cancer cell to slow down or stop cancer growth. Trastuzumab is a standard treatment for HER2-positive breast cancer
  - The chemotherapy drugs you will receive are docetaxel and carboplatin. These chemotherapy drugs are standard treatments in the United States for breast cancer. Women who take part in this study from other countries will also receive docetaxel and carboplatin and some will receive different chemotherapy drugs. This consent form only describes the chemotherapy drugs docetaxel and carboplatin that you will receive
  - A second purpose of the study is to learn if adding bevacizumab to treatment with chemotherapy and trastuzumab for HER2-positive breast cancer will prevent breast cancer from spreading to other parts of the body.
- This study will also help determine if adding bevacizumab to treatment with chemotherapy and trastuzumab will help women with HER2-positive breast cancer to live longer.
- Another purpose of the study is to learn how the combination of drugs used in this study will affect the heart.
- The researchers also want to learn about other potential side effects that might result from the combinations of drugs used in this study.

**How many people will take part in the study?**

At least 3,500 women from cancer treatment centers from all over the world will take part in this study.

**What will happen if I take part in this research study?**

*Before you begin the study:* You will need to have the following exams and tests to find out if you can be part of the study. These exams and tests are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- medical history and physical exam, including having your blood pressure checked

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- blood tests to check your blood counts and to check how well your kidneys and liver are working (blood sample of about 10 mL [1 tablespoon])
- it is possible that you will need to have a blood test to check the amount of estradiol to confirm if you are premenopausal or postmenopausal
- chest x-ray or chest CT scan
- mammogram or breast MRI
- MUGA scan or echocardiogram (to see how well your heart pumps blood)
- ECG (electrocardiogram)
- bone scan, bone x-rays, or other bone tests (only if you have bone pain or your blood tests show an increase in a bone-related protein)
- liver scan (only if your blood tests show abnormal liver function)
- if you are a woman of childbearing potential, your doctor or nurse will talk to you about having a pregnancy test
- central HER2-testing (explained to you in a separate consent form)

You will also need to have a urine sample collected before you join the study because bevacizumab may cause some patients to have abnormal amounts of protein in the urine. This test is not part of regular cancer care and is being done to make sure you are able to receive bevacizumab. If your urine contains an abnormal amount of protein, you will then need to collect your urine for 24 hours. If you need to do this, your study doctor or nurse will let you know what you need to do.

*During the study:* If all exams, tests, and procedures show that you can be in the study and if you choose to take part, you will be enrolled in the study and "randomized" to one of the two study groups described below. Randomization means that you are put into a group by chance. A computer program will place you in one of the study groups. Neither you nor your doctor can choose the group you will be in. You will have an equal chance of being placed in each group.

After you have been assigned to one of the two treatment groups, you will begin your study therapy. You will receive your study therapy on an outpatient basis on a schedule that is specific to your group. This schedule is repeated every 3 weeks. This 3-week period is called a *cycle*. The dose of each drug is based on your weight. The drugs and treatment schedules are as follows:

### **Group A study therapy**

On the first day of your treatment, you will receive docetaxel followed by carboplatin through a vein (intravenously). The day before and in the morning on the day you receive docetaxel you will take dexamethasone. Dexamethasone is a drug you take by mouth to help prevent some of the side effects of docetaxel. Also on your first day of study therapy, you will receive trastuzumab through a vein. This combination of chemotherapy and trastuzumab will be given to you once every 3 weeks for 6 cycles. For the first treatment, it will take about 3½ hours for you to receive all of the drugs. The rest of the treatments will take about 2½ hours for you to receive all of the drugs.

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After you complete the treatment cycles that include chemotherapy, you will continue to receive trastuzumab alone once every 3 weeks until about 1 year after your first dose of trastuzumab. It will take about ½ to 1 hour for you to receive trastuzumab.

**Group B study therapy**

On the first day of your treatment, you will receive docetaxel followed by carboplatin through a vein (intravenously). The day before and in the morning on the day you receive docetaxel you will take dexamethasone. Dexamethasone is a drug you take by mouth to help prevent some of the side effects of docetaxel. Also on your first day of study therapy, you will receive trastuzumab followed by bevacizumab through a vein. This combination of chemotherapy, trastuzumab, and bevacizumab will be given to you once every 3 weeks for 6 cycles. For the first treatment, it will take about 4½ - 5 hours for you to receive all of the drugs. The rest of the treatments will take about 3½ hours for you to receive all of the drugs.

After you complete the treatment cycles that include chemotherapy, you will continue to receive trastuzumab and bevacizumab once every 3 weeks until about 1 year after your first dose of these drugs. It will take about 1½ to 2 hours for you to receive both trastuzumab and bevacizumab.

Summary of study therapy:

Group A		Group B	
Docetaxel + Carboplatin + Trastuzumab	<i>Every 3 weeks for 6 cycles</i>	Docetaxel + Carboplatin + Trastuzumab + Bevacizumab	<i>Every 3 weeks for 6 cycles</i>
<i>Followed by</i>		<i>Followed by</i>	
Trastuzumab	<i>Every 3 weeks until 1 year after the first dose</i>	Trastuzumab + Bevacizumab	<i>Every 3 weeks until 1 year after the first dose</i>

Note that your doctor can modify the dose of chemotherapy or discontinue any treatment if it is necessary and useful for you.

**Other therapy**

*Hormonal therapy:* If your breast cancer is affected by hormones (estrogen or progesterone), your doctor will also give you at least 5 years of hormonal therapy beginning after your chemotherapy has been completed. Your doctor will discuss this with you.

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*Radiation therapy:* If you had breast conserving surgery (lumpectomy or partial mastectomy) or your doctor has advised radiation therapy for other reasons, you will have radiation therapy beginning after your chemotherapy has been completed. Your doctor will discuss this with you.

**Tests and exams during chemotherapy (docetaxel and carboplatin) and targeted therapy (Group A - trastuzumab and Group B – trastuzumab and bevacizumab):**

You will need to have the following tests and exams during study therapy. They are part of regular cancer care.

- physical exam, including having your blood pressure checked, before each treatment cycle
- blood tests to check your blood counts and to check how well your kidneys and liver are working before each treatment cycle (blood sample of about 10 mL [1 tablespoon] each time)
- echocardiogram or MUGA scan to check your heart function between treatment cycles 3 and 4

If the test result of this echocardiogram or MUGA scan is within the range required by the study, you will continue to receive the targeted therapy (trastuzumab with or without bevacizumab) during the remaining chemotherapy cycles. However, if the echocardiogram or MUGA scan shows a result that is below the required range, you will have a repeat echocardiogram or MUGA scan 3 weeks later to recheck your heart function. If this test result improves to within the required range, you will continue to receive the targeted therapy. If the repeat test result is still not within the required range, your targeted therapy may have to stop.

*If you are receiving bevacizumab,* you will also have a urine test before every other cycle of therapy to check for protein in your urine. If your urine contains an abnormal amount of protein, you will then need to collect your urine for 24 hours. If you need to do this, your study doctor or nurse will let you know what you need to do. These urine tests are not part of regular cancer care. They are being done for the purpose of this study.

**Tests and exams after completion of chemotherapy (Group A and Group B):**

About 2-3 weeks after your last dose of chemotherapy you will need to have the following tests and exams before continuing targeted therapy. They are part of regular cancer care.

- physical exam, including having your blood pressure checked
- blood tests to check your blood counts and to check how well your kidneys and liver are working (blood sample of about 10 mL [1 tablespoon])
- echocardiogram or MUGA scan to check your heart function

If the test result of this echocardiogram or MUGA scan is within the range required by the study, you will continue to receive the targeted therapy (trastuzumab with or without bevacizumab). However, if the echocardiogram or MUGA scan shows a result that is below the required range, the MUGA or echocardiogram will be repeated as described earlier in this

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consent form. Your doctor will either continue or stop targeted therapy depending on the results of the repeat test.

*If you are receiving bevacizumab*, before you continue receiving targeted therapy, you will have a urine test to check for protein in your urine. If your urine contains an abnormal amount of protein, you will then need to collect your urine for 24 hours. If you need to do this, your study doctor or nurse will let you know what you need to do. These urine tests are not part of regular cancer care. They are being done for the purpose of this study.

**Tests and exams during targeted therapy (after completion of chemotherapy)  
(Group A and Group B):**

You will need to have the following tests and exams. They are part of regular cancer care.

- blood pressure checks every 3 weeks
- physical exam every 6 weeks
- blood tests every 6 weeks to check your blood counts and to check how well your kidneys and liver are working (blood sample of about 10 mL [1 tablespoon] each time)
- mammogram at about 12 months after your last mammogram
- echocardiogram or MUGA scan to check your heart function at about 8 months after you join the study

If the test result of this echocardiogram or MUGA scan is within the range required by the study, you will continue to receive the targeted therapy (trastuzumab with or without bevacizumab). However, if the echocardiogram or MUGA scan shows a result that is below the required range, the MUGA or echocardiogram will be repeated as described earlier in this consent form. Your doctor will either continue or stop targeted therapy depending on the results of the repeat test.

*If you are receiving bevacizumab*, you will also have a urine test to check for protein in your urine every 6 weeks while you receive bevacizumab therapy. If your urine contains an abnormal amount of protein, you will then need to collect your urine for 24 hours. If you need to do this, your study doctor or nurse will let you know what you need to do. These urine tests are not part of regular cancer care. They are being done for the purpose of this study.

**Test and exams after completion of study therapy:**

You will need to have the following tests and exams. They are part of regular cancer care.

- physical exam, including having your blood pressure checked, every 6 months until 5 years from the time you join the study; after 5 years, physical exams, including having your blood pressure checked, will be done once a year until at least 10 years.
- mammogram every year

You will also have an echocardiogram or MUGA scan to check your heart function at about 15, 24, 36, and 60 months after you join the study. These tests are not part of regular cancer care and are being done for the purpose of this study.

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At any time, your doctor may perform any additional test or procedure to check the cancer status (CT scan, MRI, PET scan, biopsy) if it is useful for your health.

**How long will I be in the study?**

You will be in this study for at least 10 years. Your chemotherapy will last about 5 months, and the targeted therapy (trastuzumab with or without bevacizumab) will last for a total of 1 year of therapy. After you complete your study therapy, we would like to continue to follow up your health status until at least 10 years after you join the study. After the study, you will not receive any study-related care. Any care you need to receive will be from your doctor as part of regular cancer care.

**Can I stop being in the study?**

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. It is important to tell the study doctor if you are thinking about stopping so any risks from the therapy can be evaluated by your doctor. Another reason to tell your doctor is to discuss what follow-up care and testing would be the most helpful for you.

You can choose to withdraw in two ways. Either you stop your study treatment, but still allow the study doctor to report your health status until at least 10 years after you joined the study. Or, you stop your study treatment and request that no new information be reported.

Also, your study doctor may stop you from taking part in this study if he or she believes it is in the best interest of your health, if you do not follow the study rules, or if the study is stopped by the CIRG and the NSABP or health authorities.

**What side effects or risks can I expect from being in the study?**

You may have side effects while on the study. Most of these are listed here, but there may be other side effects that we cannot predict. Side effects will vary from person to person. Everyone taking part in the study will be monitored carefully for any side effects.

Side effects may be mild or very severe. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the study therapy. In some cases, side effects can be severe, long lasting, or may never go away. *There also is a risk of death.*

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**Risks and side effects related to docetaxel and carboplatin (Group A and Group B):**

***Likely***

These side effects occur in **25% or more** of patients receiving docetaxel and carboplatin:

- hair loss
- nausea
- vomiting
- taste changes
- weakness/loss of strength
- lack of energy or feeling tired
- hot flashes (in premenopausal women)
- menstrual cycles (periods) that are irregular or permanently stop
- inability to become pregnant
- skin and nail changes, including discoloration and peeling
- low number of white blood cells that may lead to infection
- anemia (low number of red blood cells that may lead to tiredness, shortness of breath)
- low number of platelets that may lead to increased bruising or bleeding
- decreased magnesium and sodium in the blood

These side effects occur in **10-24%** of patients receiving docetaxel and carboplatin:

- headache
- diarrhea
- constipation
- abdominal pain
- loss of appetite
- sores or irritation in the lining of the mouth and throat
- pain in muscles, bones, or joints
- fluid retention (bloating or swelling)
- infection
- numbness, tingling, prickling, and burning in the hands and feet
- blood test results that show changes in liver function
- decreased potassium and calcium in the blood
- allergic reaction including fever, chills, rash, itching, flushing, back pain, and shortness of breath

***Less likely***

These side effects occur in **3-9%** of patients receiving docetaxel and carboplatin:

- low number of red blood cells severe enough to require red blood cell transfusion
- blood test results that show changes in kidney function
- ulcers in the stomach or bowels
- hardening of the walls of the veins used for chemotherapy
- darkening of the soles of the feet or palms of the hands
- peeling of the skin (including hands and feet)
- eye irritation
- blurred vision
- dizziness
- blood pressure changes (high or low)

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***Rare but severe***

These side effects occur in **less than 3%** of patients receiving docetaxel and carboplatin:

- hearing loss
- liver failure
- gastrointestinal problems (such as bleeding, blockage, or perforation [opening of a hole] in the stomach or bowel)
- skin and tissue damage in the area surrounding the catheter used to give the chemotherapy drugs
- acute leukemia (cancer of the blood cells)
- blood clot in a blood vessel
- heart problems
- lung problems
- severe infection
- inflammation of the pancreas causing abdominal pain
- severe allergic reaction including chills, rash, itching, flushing, low blood pressure, wheezing, and shortness of breath
- a group of symptoms which may include a blister-like rash that may be severe enough to require hospitalization; fever; inflamed eyes; redness, swelling, and painful sores on lips and in mouth (Stevens-Johnson Syndrome)

**Risks and side effects related to trastuzumab (Group A and Group B):**

***Likely***

These side effects occur in **25% or more** of patients receiving trastuzumab:

- weakness
- fever
- headache
- diarrhea
- pain
- chills
- nausea
- cough

These side effects occur in **10-24%** of patients receiving trastuzumab:

- abdominal pain
- back pain
- loss of appetite
- dizziness
- shortness of breath
- infection
- vomiting
- difficulty sleeping
- skin rash or ulceration
- allergy-type symptoms like sneezing, nasal stuffiness, and postnasal drip

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***Less likely***

These side effects occur in **3-9%** of patients receiving trastuzumab:

- sore throat
- flu-like symptoms
- anemia (low number of red blood cells that may lead to tiredness, shortness of breath)
- blood test results that show changes in liver function
- low number of white blood cells that may lead to infection
- reaction to the infusion including: fever, chills, hives, rash, joint pain, pain at the tumor site, shortness of breath, low or high blood pressure, and sweating may occur during the infusion and last about 24 hours
- decreased ability of the heart to pump blood. If severe, you could have shortness of breath and other symptoms of heart failure. (If mild, you may not have any symptoms.)
- swelling
- rapid or irregular heartbeat
- depression
- allergic reaction (including chills, rash, hives, itching, flushing, swelling, low blood pressure, wheezing, and shortness of breath)
- pain in the chest area
- pain in the muscles, bones, and joints

***Rare but severe***

These side effects occur in **less than 3%** of patients receiving trastuzumab:

- severe reaction to the infusion
- severe allergic reaction
- blood clot in a blood vessel
- severe lung problems (including shortness of breath, fluid in the lungs, low levels of oxygen in the blood, and damage that could be permanent)

**Risks and side effects related to bevacizumab (Group B):**

The following side effects were seen when bevacizumab was given together with chemotherapy or other therapies. This does not mean that these side effects were necessarily caused by bevacizumab.

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***Likely***

These side effects occur in **10% or more** of patients receiving bevacizumab:

- nausea
- vomiting
- diarrhea
- constipation
- dehydration
- loss of appetite
- taste changes
- protein in the urine
- increased tears in the eyes
- runny nose
- nose bleed
- inflammation of the lining of mouth
- lack of energy or feeling tired
- shortness of breath
- peripheral sensory neuropathy (for example, numbness or loss of feeling in the fingers or toes, or problems doing ordinary things with your fingers, like buttoning a shirt)
- fainting
- fever
- high blood pressure
- hand-foot syndrome (pain or blistering on the hands or feet)
- dry skin, flaking and inflammation of the skin, change in skin color
- pain
- infection in the blood or bladder
- low number of white blood cells, sometimes associated with fever, that may result in infection
- bleeding from the rectum

***Less likely***

These side effects occur in **3-9%** of patients receiving bevacizumab:

- abdominal pain
- blockage in the intestine
- anemia (low number of red blood cells that may lead to tiredness, shortness of breath)
- bleeding from the lining of the mouth or vagina
- blood clots in the veins of the legs
- pulmonary embolism (blood clot in a vessel in the lung)
- blocking of an artery by a blood clot, which can lead to a stroke or heart attack
- problems with the heart or increase in heart rate (pulse)
- heart failure, especially in patients who have taken certain chemotherapy treatments in the past
- increased blood sugar
- allergic reaction including reactions during the infusion (including chills, rash, hives, itching, flushing, swelling, low blood pressure, wheezing, and shortness of breath)
- decreased blood potassium
- decreased blood phosphorous
- decreased sodium
- increased blood alkaline phosphatase

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***Rare but severe***

These side effects occur in **less than 3%** of patients receiving bevacizumab:

- low number of platelets (that may lead to increased bruising or bleeding)
- low levels of oxygen in the blood
- perforation of the gastrointestinal tract (a tear or a hole in the gut) that may be associated with an abdominal abscess or infection
- fistula (an abnormal tube-like connection between internal organs and skin or other tissues that are not normally connected) may occur, for example, between the gastrointestinal tract and the skin or between the gastrointestinal tract and the vagina. A rare type of fistula (tracheo-esophageal) is described below.
- tracheo-esophageal fistula (an abnormal connection between the windpipe (trachea) and the esophagus (the tube that connects the mouth to the stomach))
- bleeding, including bleeding associated with the gastrointestinal tract or bleeding in the brain or coughing up blood
- reversible posterior leukoencephalopathy syndrome (RPLS) or hypertensive encephalopathy. This may include symptoms of impaired brain function (headaches, vision changes, confusion, or seizures), and often, high blood pressure.
- delay in wound healing, failure of a wound to heal or spontaneous opening of a wound. You should inform your doctor if you are considering surgery.
- hole in the nasal passage (nasal septum perforation)
- weight loss (not all patients had severe weight loss)

*Talking with your doctor about side effects:* Some side effects are more common in elderly patients than in younger patients. These side effects include blood clots in the arteries which can lead to a stroke or a heart attack. In addition, elderly patients have a higher risk of a reduction in the number of white cells in the blood.

It is important that you contact your doctor as soon as you experience any side effects whether you think the treatment has caused them or not. You must also tell your doctor if you have any illnesses or if you have started any new medication. This includes medications available without a prescription (over the counter) and alternative medicines. If you have any questions or concerns about any of the information provided above, about the possible side effects of treatment, or the possible consequences of treatment for those side effects, please ask your study doctor or research staff for more information.

The most important symptoms you need to report to your doctor immediately are allergy, possible infusion reactions (symptoms that start within a few hours of the infusion, e.g., wheezing, tightness in the throat or chest, rash, and facial swelling), bleeding, and high fever. This last symptom may be a sign of a serious infection associated with an impaired immune system, and impaired brain function (e.g., dizziness, blurred vision, confusion). **If you**

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**experience any severe side effect**, you should seek professional medical help immediately. Call your study doctor and, if necessary, go to the nearest emergency room.

*Risks related to fertility and pregnancy:* The drugs in this study can affect an unborn baby. Therefore, you should not become pregnant and must use an effective non-hormonal method of contraception during therapy and for at least 6 months after your last dose of bevacizumab and/or trastuzumab. You should ask about counseling and more information about preventing pregnancy. If you feel you might be pregnant, even though you practiced birth control, contact your study doctor immediately who will talk with you about the appropriate action to be taken. A pregnancy test may be performed.

Also, you should not breastfeed a baby during therapy and for at least 6 months after your last dose of bevacizumab and/or trastuzumab. Some of the drugs used in this study may affect your ability to have children in the future.

*General risks and side effects:* Drawing blood samples may cause bruising (black and blue marks) and discomfort where the blood was taken. There is also a possibility of infection or blood clots at the site of the blood draw.

If your doctor checks your heart function with MUGA scans, or if you need to have a CT scan or other type of imaging study, there is a potential risk of radiation exposure, however, this risk is considered small.

For more information about risks and side effects, ask your study doctor.

### **Are there benefits to taking part in the study?**

Taking part in this study may or may not make your health better. While doctors hope that adding bevacizumab to standard therapy will be more useful in the treatment of HER2-positive breast cancer, there is no proof of this yet. We do know that the information from this study will help doctors learn more about bevacizumab given with standard therapy for HER2-positive breast cancer. This information could help future breast cancer patients who may receive similar treatment.

If at any time during the study, the treatment is no longer effective or causes serious side effects, the study treatment may be stopped and your study doctor will discuss with you further treatment and best management of your disease.

### **What other choices do I have if I do not take part in this study?**

Your other choices may include:

- Getting treatment or care for your cancer without being in this study
- Getting the treatment described as Group A in this consent form without being in this study
- Taking part in another study, if available

Talk to your doctor about your choices before you decide if you will take part in this study.

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Your decision will not affect your relationship with the medical team and the future management of your disease.

**What are my responsibilities?**

- Keep your study appointments. If you cannot keep an appointment, contact your study doctor or research study staff to reschedule as soon as you know that you will miss the appointment.
- Tell your study doctor or research staff about any medications you are taking.
- Tell your study doctor or research study staff about any side effects, doctor visits, or hospitalization that you may have whether or not you think they are related to the study therapy.
- Tell your study doctor or research staff if you believe you might be pregnant.
- While participating in this research study, you should not take part in any other research project without approval from your study doctor. This is to protect you from possible injury arising from such things as extra drawing of blood samples, possible incompatibility between research drugs, or other hazards.
- You should inform your study doctor or research staff if you are considering surgery.

**Will my medical information be kept private?**

All the data obtained during the study that concern you will be treated as confidential and will not be made publicly available. You will be identified only by a unique code number and information about the code will be kept in a secure location and access limited to research study personnel. The data will be coded, stored, and protected.

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law.

These data will be analyzed to determine whether and how the drug has worked in you and the other people in the study. The results of the study may be forwarded to health authorities worldwide and the results may also be used in reports of the study or for presentations at scientific or medical meetings or published in scientific journals. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. The results of this study may be used for future medical research.

By agreeing to participate in this study, the following organizations may have confidential access to your medical records for research, quality assurance, and data analysis:

- the Cancer International Research Group (CIRG), including monitors and auditors;
- the National Surgical Adjuvant Breast and Bowel Project (NSABP), including auditors;
- F. Hoffmann-La Roche Ltd. (including auditors), a company that is providing support for the trial;

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- Genentech, Inc. (including auditors), a company that is providing support for the BETH Trial;
  - Quintiles (including monitors and auditors), a company that will monitor the centers taking part in the BETH Trial;
  - the CIRG Central Laboratory;
  - the Marquette General Hospital Institutional Review Board (IRB), a local group of people who reviewed and approved the research study to protect your rights
  - government agencies including, the FDA and the Office for Human Research Protections (OHRP). These agencies may review the research to see that it is being done safely and correctly
- **What are the costs of taking part in this study?**

You and/or your health plan/insurance company will need to pay for some or all of the costs of treating your cancer in this study. Some health plans will not pay for these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

*Tests, procedures, or drugs for which there is no charge in this study:*

- All urine tests to check for protein. These tests will be done before you join the study and at the scheduled time points described earlier in this consent form.
- The echocardiogram or MUGA scan performed at 15, 24, 36, and 60 months after you join the study
- Bevacizumab will be provided for this study at no cost to you by Genentech, Inc. or F. Hoffmann-La Roche Ltd. However, you or your health plan will need to pay for the costs of supplies and personnel who give you the drug.

Bevacizumab is the common name for the commercial drug Avastin®. The bevacizumab used in this trial, however, is for use in research studies only and may be made at locations different from those where Avastin is made. Although some differences may exist, bevacizumab for research use and the commercial drug, Avastin, are manufactured by a similar process, meet similar standards for final product testing, and are expected to be very similar in safety and effectiveness.

Docetaxel, carboplatin, and trastuzumab are commercially available and will not be provided for free with this study. You and/or your health plan/insurance company will be responsible for the costs of these drugs and for the supplies and the personnel required to give these drugs.

As described to you in a separate consent form, there will be no charge to you or your insurance company for the collection, shipping, or HER2 testing of your tumor sample that is required for the BETH Trial.

Patient's Initials: \_\_\_\_\_

You will not be paid for taking part in this study. Taking part in this study may result in added costs to you.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at <http://www.cancer.gov/clinicaltrials/understanding/insurance-coverage>. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site. Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

**What happens if I am injured because I took part in this study?**

It is important that you tell your study doctor, \_\_\_\_\_, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at \_\_\_\_\_.

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment and no compensation will be provided.

**What are my rights if I take part in this study?**

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from your center.

The Independent Data Monitoring Committee (IDMC), an independent group of experts, will be reviewing the data from this research throughout the study. We will tell you and your doctor about new information or changes in the study that may or may not affect your health or your willingness to continue in the study. You may be asked to sign another consent form in response to new information.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

**Who can answer my questions about the study?**

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor \_\_\_\_\_ at \_\_\_\_\_.

For questions about your rights while taking part in this study, call Marquette General Hospital at 906-228-9440 and ask to speak with the Patient Advocate.

Patient's Initials: \_\_\_\_\_

## **Additional Tests for the BETH Trial**

### **What about the use of my tumor for research?**

***About using tumor for research:*** If you voluntarily agree, remaining tumor sample after the required HER2 testing, which was described in a separate consent form, will be kept for use in this study and for research to learn more about cancer and other diseases. Use of your tumor sample after the HER2 testing is not required for participation in the BETH Trial.

The research that will be done with your tumor samples is not designed to specifically help you. It might help people who have cancer in the future. Reports about research done with your samples will not be given to you or your doctor. These reports will not be put in your health records. The research using your tumor samples will not affect your care. These tumor samples will not be used for genetic research about diseases that are passed on in families.

The BETH Trial researchers (the CIRG, the NSABP, and F. Hoffmann-La Roche Ltd.) will study the samples and may give them to other researchers. Any research using your samples must also be approved by an IRB. An IRB is a group of people who review the research to determine if it is being done correctly and safely.

People who do research with your tumor samples may need to know more about your health. While the CIRG and the NSABP may give them reports about your health, they will not give them your name, address, phone number, or any other information that will let the researchers know who you are.

Your tumor samples will be used only for research and will not be sold. The research done with your samples may help to develop new products in the future, but you will not be paid.

If you decide now that your tumor samples can be kept for research, you can change your mind at any time. Just *contact your study doctor* and let him or her know that you no longer want your tumor samples to be used, and they will no longer be used for research. Otherwise, your tumor samples may be kept until they are used up, or until they are destroyed.

***Benefits and risks:*** The possible benefits of research from your tumor samples include learning more about what causes cancer and how to treat it.

There is a risk of the release of information from your health records. The CIRG and the NSABP will protect your records so that your name, address, and phone number will be kept private. The chance that this information will be given to someone else is very small.

***Costs of the sample collections:*** There will be no cost to you for the collection and storage of the optional tumor samples in this study.

Patient's Initials: \_\_\_\_\_

### **Making your choices**

Please read each statement below and think about your choice. After reading each statement, circle “yes” or “no.” If you have questions, please talk to your doctor or health care team member.

*Participation in the optional tumor submission:* Remember, no matter what you decide about the **optional** collection and use of the tumor samples in this research study, you may still take part in the BETH Trial.

1. My tumor samples may be kept for the research purposes of the BETH Trial.

YES                      NO

2. My tumor samples may be kept for use in future research to learn about, prevent, or treat cancer.

YES                      NO

3. My tumor samples may be used for research about other health problems (for example: causes of diabetes, Alzheimer's disease, or heart disease).

YES                      NO

*Contact in the future for other research:* Remember, no matter what you decide, you may still take part in the BETH Trial.

4. My study doctor (or someone he or she chooses) may contact me in the future to ask me to take part in more research.

YES                      NO

### **Where can I get more information about cancer and its treatment?**

You may call the National Cancer Institute’s (NCI’s) Cancer Information Service at: 1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615.

You may also visit the NCI Web site at <http://cancer.gov>

- For the NCI’s clinical trials information, go to: <http://cancer.gov/clinicaltrials>
- For the NCI’s general information about cancer, go to: <http://cancer.gov/cancerinfo>

You may also visit the NSABP Web site at <http://www.nsabp.pitt.edu>

Patient’s Initials: \_\_\_\_\_

You will receive a copy of this consent form. If you want more information about this study, ask your study doctor.

**Signatures**

I have been given a copy of all nineteen pages of this form. I have read the patient informed consent form or it has been read to me. This information was explained to me and my questions were answered.

I consent to take part in this research study.

\_\_\_\_\_  
Date

\_\_\_\_\_  
Patient's signature

\_\_\_\_\_  
Printed name of patient

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature of person conducting the  
informed consent discussion

\_\_\_\_\_  
Printed name of person conducting the  
informed consent discussion

Patient's Initials: \_\_\_\_\_