

**MARQUETTE GENERAL HEALTH SYSTEM**  
Regional Medical Center

CONSENT TO PARTICIPATE IN AN INVESTIGATIONAL STUDY

**TITLE: SCUSF 0806 “Phase II placebo-controlled trial of lisinopril and Coreg CR® to reduce cardiotoxicity in patients with breast cancer receiving (neo) adjuvant chemotherapy with trastuzumab (Herceptin®) ”**

**INVESTIGATORS:** Sheetal Acharya, MD  
Amy Bolmer, DO  
Rifat Elkhatib, MD  
Santosh Gowda, MD  
Gustavo Morel, MD  
Ross Siemers, MD  
Amy M. Weise, DO  
1414 W. Fair Avenue  
Marquette, MI 49855

**SPONSOR:** SunCoast CCOP Research Base

This consent form gives you detailed information about the research study which the doctor will discuss with you. The purpose of this study includes evaluation of the safety as well as the effectiveness of the investigational therapy.

***Introduction:***

**This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose 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.**

You are being asked to take part in this study because you have been diagnosed with breast cancer and are scheduled to start trastuzumab (Herceptin®), which can cause problems with heart function.

### ***Why is this study being done?***

**The purpose of this study is to** compare the effects, good and/or bad, of an ACE inhibitor (lisinopril) or a beta-blocker (Coreg CR® [carvedilol phosphate extended release]) on heart function during treatment with trastuzumab (Herceptin®), a drug you will receive as treatment for your breast cancer. Lisinopril and Coreg CR® are used to treat high blood pressure, heart failure and in heart attack patients. Study doctors want to find out which treatment (lisinopril or Coreg CR®) is better at protecting heart function during treatment of breast cancer. The effect of the medicines will be compared to a placebo, which contains no active drug. You will only get one of the study medicines (lisinopril, Coreg CR® or placebo).

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

About 468 people 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, tests or procedures to find out if you can be in the study. These exams, tests or procedures may be done on an outpatient basis, 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 examination, including height and weight
- A measurement of your heart function to see how strong it pumps. This can be done using a MUGA scan or an echocardiogram (ECHO). The best testing method for you will be decided by your doctor.
- Blood tests checking your heart, liver and kidney functions

**During the study ...**

**If the exams, tests and procedures show that you can be in the study, and you choose to take part, then you will need the following tests and procedures. They are part of regular cancer care.**

- Physical examination, including height and weight every 3 months (+/- 2 weeks) for 52 weeks (or until the end of trastuzumab, if it is given for less than 1 year),

at study months 18 and 24 (or 6 months and 12 months after the last dose of trastuzumab).

- Heart function test (MUGA scan or ECHO) every 3 months (+/- 2 weeks) for 52 weeks (or until the end of trastuzumab, if it is given for less than 1 year), at study months 18 and 24 (or 6 months and 12 months after the last dose of trastuzumab).
- Follow up additional research visits to see how you are doing and to review your regular list of medicines will be conducted at study months 15 and 21 (or 3 and 9 months after ending trastuzumab).

**You will need these procedures that are either being tested in this study or being done to see how the study is affecting your body.**

- Complete a quality of life questionnaire before you start the study, when you finish taking 1 year (52 weeks) of study agent (or when trastuzumab ends, if it is given for less than 1 year) and at study months 18 and 24 (or 6 months and 12 months after the last dose of trastuzumab). It takes about 10 minutes to complete the questionnaire.
- Take a pill (study medicine) by mouth with food once every day for one year (52 weeks) or until trastuzumab ends (if it is given for less than one year).
- Keep a written record (Study Medicine Daily Log) of each time you take the study medicine. This record also has a place for you to write down any side effects you are having. This will only take a few minutes each day.
- Bring the Study Medicine Daily Logs to each study follow-up visit when you see your study doctor (at least every 3 months (+/- 2 weeks)).
- Heart function test (MUGA scan or ECHO) every 3 months (+/- 2 weeks) while taking trastuzumab and study medicine.
- Have blood tests to check your heart, liver and kidney function every 3 months (+/- 2 weeks) for 1 year (52 weeks) or at the end of trastuzumab, if it is given for less than 1 year) and at study months 18 and 24 (or 6 months and 12 months after the last dose of trastuzumab).
- You will be taught to take your blood pressure every day during the first week of study medicine, three times during the second week and then once every week until you finish taking study medicine. The SunCoast CCOP Research Base will supply blood pressure cuffs at no cost to the patient.

**You will be "randomized" into one of the three (3) 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. You will have an equal chance of being placed in any group. All study medicines look the same; and, neither you nor your doctor will know which treatment you receive. This is referred to as a "double-blinded" study.**

**One group will be randomized to receive lisinopril, an ACE inhibitor. The study drug will be taken by mouth one time each day with food.**

**One group will be randomized to receive Coreg CR®, a beta-blocker. The study drug will be taken by mouth one time each day with food.**

**One group will be randomized to receive a placebo (no active drug) to take by mouth one time each day with food.**

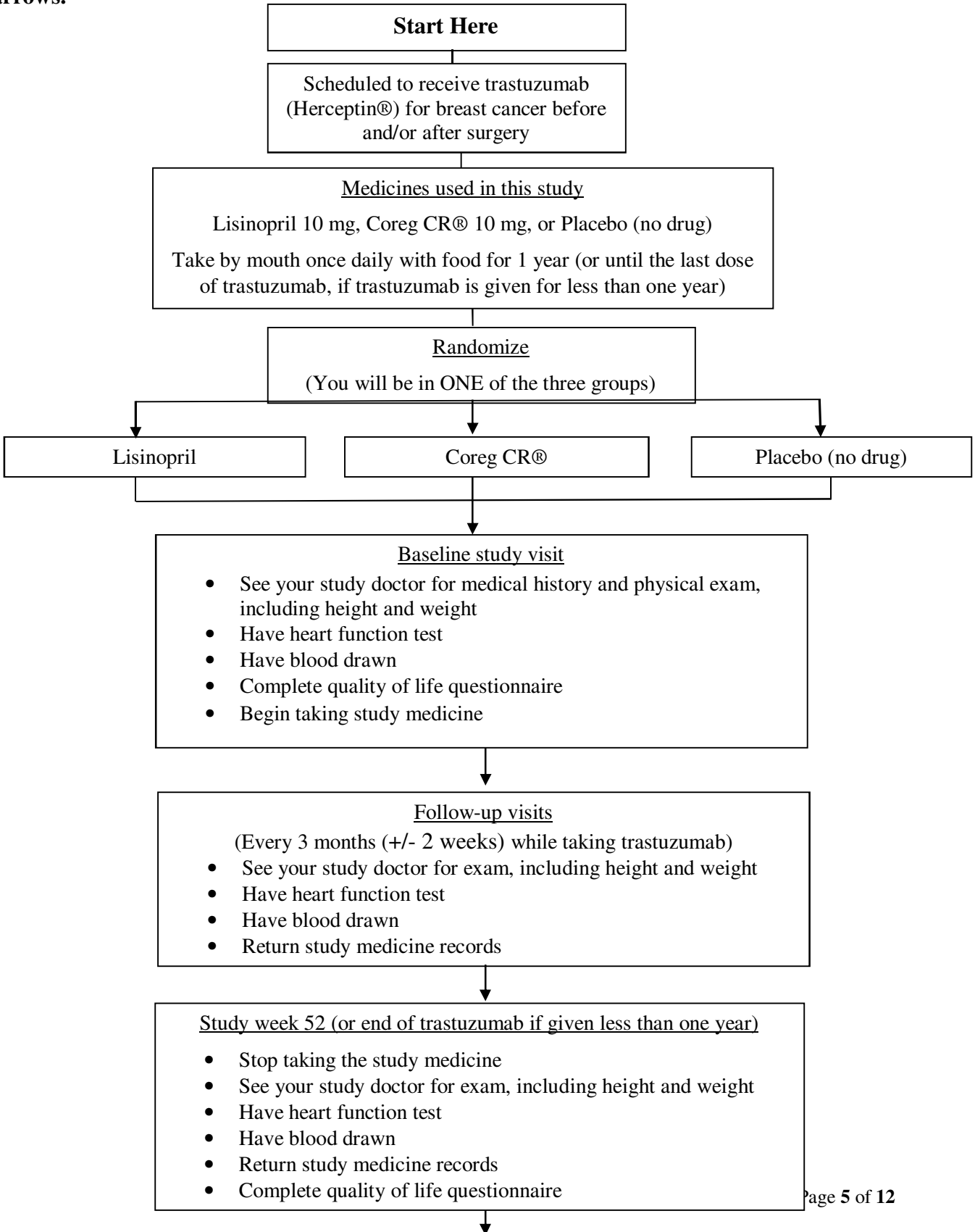
**When I am finished taking study medicine**

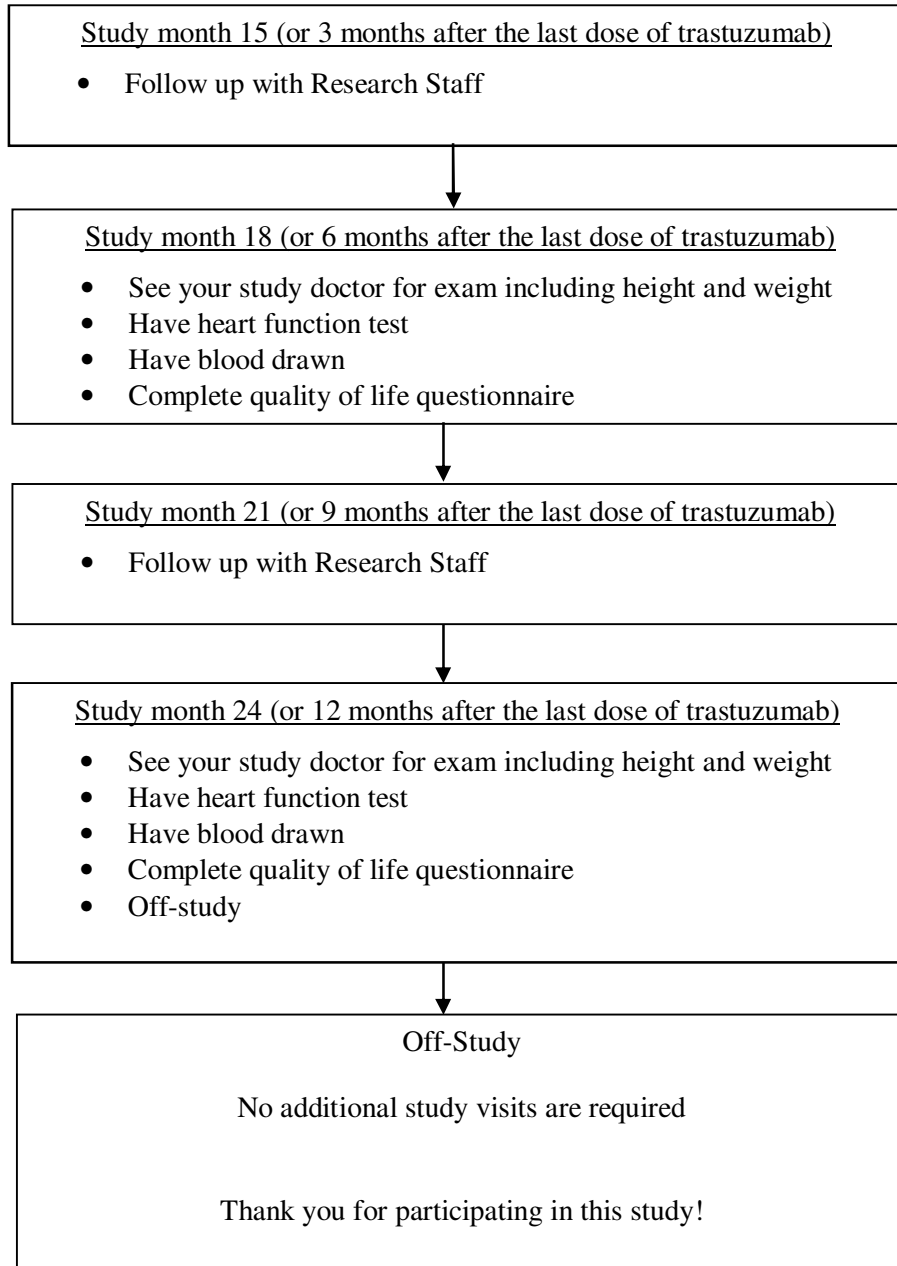
You will stop taking the study medicine (lisinopril, Coreg CR®, or placebo) at the end of one year (52 weeks) OR when your treatment with trastuzumab ends (if it ends before one year of therapy); however, you will continue to be followed on study for 1 more year. Research staff will meet with you at least once every 3 months while you are being followed on the study.

Your last study visit will be at study month 24 (or 12 months after ending trastuzumab therapy, if it was given for less than one year).

## STUDY PLAN

Another way to find out what will happen to you during the study is to read the chart on the next page. Start reading at the top and read down the list, following the lines and arrows.





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

**You will be asked to take** lisinopril or Coreg CR® or placebo by mouth once daily with food for 1 year, or until the last dose of trastuzumab (if therapy ends in less than one year). You will be seen in the clinic every 3 months (2 weeks) while you are taking study medicine. After you are finished taking the study medicine (lisinopril or Coreg CR® or placebo), you will be seen every 3 months for one more year to evaluate heart function and to see how you are doing, as described above and as shown in the study plan table. The 24 month visit completes the study; and, no additional follow-up is required for study purposes.

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

**Yes. You can decide to stop at any time.** However, these study medicines should not be stopped abruptly. **Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.**

**It is important to tell the study doctor if you are thinking about stopping so any risks from lisinopril or Coreg CR® can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.**

**The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest; if you do not follow the study rules; or if the study is stopped.**

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

**You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking lisinopril or Coreg CR® or placebo. In some cases, side effects can be serious, long lasting, or may never go away. There is also a risk of death.**

**You should talk to your study doctor about any side effects that you have while taking part in the study.**

**Risks and side effects related to the study medicines, lisinopril and Coreg CR® include those which are:**

**Lisinopril:**

<b>Likely: (&gt; 20%)</b>	<b>Less Likely: (&lt; 20%)</b>	<b>Rare but Serious:</b>
<p>No side effects have been reported frequently enough to be considered “likely to happen” while taking lisinopril</p>	<ul style="list-style-type: none"> <li>• Cough</li> <li>• Hypotension (lower blood pressure)</li> <li>• Dizziness</li> <li>• Headache</li> <li>• Fatigue</li> <li>• Diarrhea</li> </ul>	<ul style="list-style-type: none"> <li>• Rapid swelling of the face, lips, tongue, and throat (called angioedema); or swelling of the intestine (intestinal angioedema) Life-threatening allergic reactions have been reported in patients allergic to venom from yellow jackets, wasps, hornets, bees and stinging ants. This is called immune hypersensitivity reaction.</li> <li>• Increased levels of blood urea nitrogen and creatinine, which indicates there may be problems with kidney function</li> <li>• High blood levels of potassium, an electrolyte that can affect the heart</li> <li>• Inflammation of the pancreas (pancreatitis)</li> <li>• Severe skin rash</li> </ul>

**COREG CR® (carvedilol phosphate, extended-release)**

Likely: (> 20%)	Less Likely: (< 20%)	Rare but serious:
<ul style="list-style-type: none"> <li>• Dizziness</li> <li>• Fatigue</li> </ul>	<ul style="list-style-type: none"> <li>• Slow heart rate</li> <li>• Low blood pressure</li> <li>• Headache</li> <li>• Fainting</li> <li>• Weakness</li> <li>• Cough</li> <li>• Diarrhea</li> <li>• Nausea and vomiting</li> <li>• Weight gain</li> <li>• High blood sugar</li> <li>• Chest pain</li> <li>• Swelling in the legs/feet (peripheral edema)</li> <li>• Pain in the joints (Arthralgias)</li> <li>• Abnormal vision</li> <li>• High cholesterol</li> </ul>	<ul style="list-style-type: none"> <li>• Status asthmaticus (severe asthma symptoms that may result in death)</li> <li>• Low platelet count can increase bleeding tendencies</li> <li>• Severe skin rash</li> <li>• Abnormal liver function tests</li> <li>• Normal allergic reactions to known allergens (e.g. bee venom) may be exaggerated while taking Coreg CR®</li> <li>• Bronchospasm with difficulty breathing</li> </ul>

**Reproductive risks: You should not be pregnant when starting this study or become pregnant while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important you understand that you need to use birth control while on this study. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study. If you could be pregnant, tell your study doctor.**

**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 the medicines used in this study will be useful in preventing injury to your heart from your cancer treatment, there is no proof of this yet. We do know that the information from this study will help doctors learn more about lisinopril and Coreg CR® as a treatment to help protect your heart during chemotherapy. This information could help future cancer patients.**

***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 a study**
- **Taking part in another study**
- **Getting no treatment**

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

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

**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. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.**

**Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:**

- **Marquette General Hospital Institutional Review Board**
- **The SunCoast CCOP Research Base**
- **The Cancer Trials Support Unit (CTSU), a service sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials, may also view your records if you are participating in this trial through one of their institutions**
- **The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people**

***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 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 you or your insurance company more than the cost of getting regular cancer treatment.**

The study sponsor, The SunCoast CCOP Research Base, is supplying study medicine at no cost to you. The study-specific laboratory testing, the heart function studies that are not considered standard of care and the EORTC QLQ-C30 Quality of Life forms are also supplied by the SunCoast CCOP Research Base at no cost to you. The SunCoast CCOP Research Base is supplying a blood pressure cuff at no cost to you. The SunCoast CCOP Research Base does not cover the cost of getting the lisinopril, Coreg CR or placebo ready and giving it to you, so you or your insurance company may have to pay for this.

**You will not be paid for taking part in this study.**

**For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at <http://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 the Marquette General Hospital Patient Advocate at 1-906-225-3183 or 1-800-562-9753, extension 3183.**

**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.**

***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 our institution.**

**We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.**

**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 the Marquette General Hospital Patient Advocate at 1-906-225-3183 or 1-800-562-9753, extension 3183.**

***Where can I get more information?***

**You may call the National Cancer Institute'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 NCI's clinical trials information, go to: <http://cancer.gov/clinicaltrials/>**
- **For NCI's general information about cancer, go to <http://cancer.gov/cancerinfo/>**

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

**Signature**

**I have been given a copy of all 12 pages of this form. I have read it or it has been read to me. I understand the information and have had my questions answered. I agree to take part in this study.**

**Participant \_\_\_\_\_**

**Date \_\_\_\_\_**