

MARQUETTE GENERAL HEALTH SYSTEM

Regional Medical Center

CONSENT TO PARTICIPATE IN AN INVESTIGATIONAL STUDY

TITLE: CHARTED: ChemoHormonal Therapy versus Androgen Ablation Randomized Trial for Extensive Disease Prostate Cancer

Version Date: June 15, 2011

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

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.

This is a clinical trial, a type of research study. Your 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 doctor for more explanation.

You are being asked to take part in this study because you have prostate cancer that has spread beyond the prostate and can be seen on scans.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to evaluate a new way of treating patients with prostate cancer. In Arm A, you will receive docetaxel chemotherapy both at the time you are starting hormonal therapy and later when/if the hormonal therapy is no longer working per your doctor decision. In Arm B, patients only get chemotherapy when/if the hormonal therapy is no longer working per your doctor decision. We are doing the study to see if there is a benefit to giving chemotherapy at the beginning. Hormonal

therapy refers to drugs or surgical procedures such as an orchiectomy (removal of testicles) which lower your testosterone. This puts prostate cancer into remission in most patients as the testosterone is like a fuel for the cancer. It is the standard to give this as the only treatment for your cancer. Normally chemotherapy is reserved for when a patient's cancer starts to grow again despite having a low testosterone level. In this study you will either get docetaxel when you start your hormonal therapy or when/if your cancer grows with a low testosterone level. If you have chemotherapy when you start hormones for the first time, you may get chemotherapy when/if your cancer grows back with a low testosterone level.

If your disease worsens while you are on hormone treatments, your doctor will consider your next treatment very carefully. This protocol has asked, but not required, that your doctor use docetaxel (a type of chemotherapy) once your disease worsens, even if you had received docetaxel when you started hormone therapy. Your doctor may also try another hormone treatment before starting you on docetaxel chemotherapy. The purpose of this study is to determine whether receiving docetaxel both when you start hormone therapy (or within 120 days of beginning hormonal therapy) as well as when your disease worsens, is better than only receiving docetaxel when your disease gets worse. This trial will let us know which approach is more effective in treating your disease.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 600 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 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 doctor.

- Physical Examination with medical history and vital signs
- Blood tests
- Scans of the body (bone scan, chest scan, chest x-ray, abdomen/pelvis scan)

You will be "randomized" into one of the 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 a *one in two* chance of being placed in the group that receives chemotherapy when starting hormonal therapy (Group A). Group B patients will be treated with hormonal therapy alone.

Hormonal therapy refers to lowering of your testosterone and can be done by removal of testicles or injections (“shots”). Chemotherapy is normally given at the time the cancer learns to grow without testosterone. This study is trying to see if people’s cancer can be controlled for longer if chemotherapy is given when starting hormonal therapy and what the effect the chemotherapy has on a patient’s quality of life.

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.

If you are to receive chemotherapy immediately, you will have the following done every 3 weeks, prior to your infusion:

- Physical Examination, vital signs
- Blood tests

If you are to receive hormonal therapy alone, you will have the following tests every 12 weeks:

- Physical Examination, vital signs
- Blood test

WHEN YOU ARE FINISHED TAKING CHEMOTHERAPY

You will be followed every 3 months for a doctor visit to assess the status of your health and your cancer.

STUDY CHART

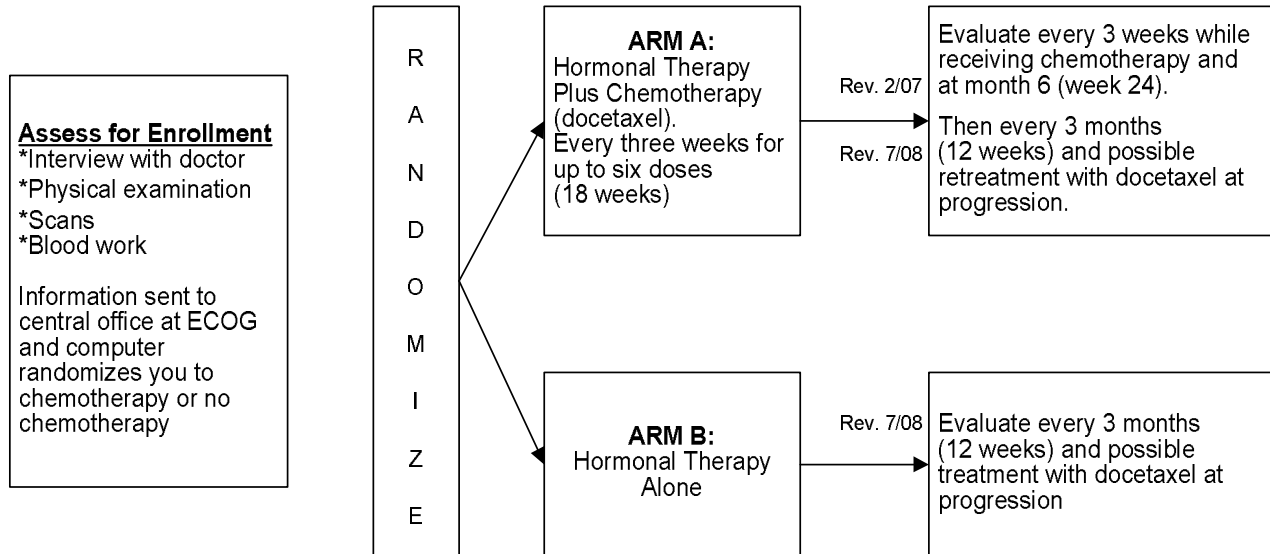
Study Chart

You will receive hormonal therapy (treatments to lower testosterone) continuously and if you are randomized to receive chemotherapy when starting hormonal therapy, you will get docetaxel every three weeks for up to 6 doses in this study. This three week period of time is called a cycle. The cycle will be repeated six times. Each cycle is numbered in order. The chart below shows what will happen to you during Cycle 1 and future treatment cycles as explained previously if you are to receive chemotherapy when you start hormonal therapy. The left-hand column shows the day in the cycle and the right-hand column tells you what to do on that day.

Day	Cycle 1-6	What you do
Just before chemotherapy		<ul style="list-style-type: none">• Take dexamethasone (pre-medication to prevent reactions from chemotherapy) 12 hours, 3 hours and 1 hour prior to infusion
Day 1		<ul style="list-style-type: none">• Check into doctor's office, get blood tests and if suitable, get chemotherapy

If you are randomized to hormonal therapy alone, you will come to the doctor's office and be followed and receive "hormone" shots if your testicles were not removed. Chemotherapy is to be reserved for when your cancer progresses with a low testosterone.

Study Plan



HOW LONG WILL I BE IN THE STUDY?

We think you will be in the study for several months.

We would like to keep track of your medical condition for 10 years to look at the long-term effects of the study.

CAN I STOP BEING IN THE STUDY?

Yes. You can decide to stop at any time. Tell the 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 doctor if you are thinking about stopping so any risks from the chemotherapy and/or hormonal therapy 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 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 the chemotherapy and/or hormonal therapy. In some cases, side effects can be serious, long lasting, or may never go away. Death is rare, but possible.

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

Risks and side effects related to the study include those which are:

Docetaxel (Taxotere)

Likely

- Nausea, vomiting or diarrhea
- Lowered white blood cell count (may make you more likely to get an infection)
- Lowered platelets (may make you more likely to bruise or bleed)
- Lowered red blood cell count (may make you feel tired or weak)
- Numbness and pain of the hands and feet
- Hair loss
- Muscle weakness/muscle and joint aches
- Mild to severe allergic reaction at the time the infusion is given
- Nail changes - drying and lines
- Fluid in arms and/or legs
- Changes in liver enzymes
- Fever
- Skin rash or dry skin
- Loss of appetite
- Taste changes
- Fatigue (feeling tired)

Less Likely

- Shortness of breath
- Sores in the mouth or throat

- Itching
- Headaches
- Fluid around the heart or the lungs
- Changes in kidney function tests which may lead to stopping docetaxel
- Low blood pressure
- Irregular heart beat (arrhythmias) or heart failure
- Skin irritation, redness, heat, swelling and pain at the site of injection of the medication
- Redness or irritation of the skin at a prior site of radiation therapy
- Irritation of the eye
- Low blood sodium level
- An abnormally high level of the simple sugar glucose in the blood
- Inflammation of the esophagus (the passageway between the mouth and the stomach)
- Inflammation of the pancreas (a small gland behind the stomach that secretes substances such as insulin)

Rare, but serious

- Seizures
- Blood clots
- Damage to the intestines which could be life-threatening
- Liver damage or failure

LHRH agonists (such as leuprolide, goserelin, triptorelin)

Likely

- Hot flashes
- Swelling caused by fluid held in the tissues
- Abnormal enlargement of male breasts
- Bone pain, loss of bone density
- Blood clotting within blood vessels.
- Gastrointestinal (stomach) disturbances – diarrhea, nausea, vomiting

Less Likely

- The inability to achieve an erection or have sexual intercourse.
- Loss of sexual desire
- Weight loss
- Weight gain
- Depression
- Increase in liver enzyme

- Dizziness
- Headache
- Decreased number of red blood cells
- Increased thirst and urination
- Unusual taste in mouth

Rare, but Serious

- Rash due to allergic reaction
- Difficulty breathing

Antiandrogens (flutamide and bicalutamide)

Likely

- Abnormal enlargement of male breasts
- Diarrhea
- Nausea, vomiting
- Decreased number of red blood cells
- Breast tenderness and swelling
- Hot flashes
- High blood pressure

Less Likely

- Elevated level of liver enzymes indicating liver injury
- Too much bile in the blood causing a yellow color to the skin, gums, eye, and other tissues
- The inability to achieve an erection or have sexual intercourse.
- Loss of sexual desire
- Fatigue

Rare, but Serious

- Death due to liver failure
- A condition in which the skin is overly sensitive to light

Reproductive risks: You should not become pregnant or father a baby while on this study because the drugs in this study can affect a fetus. 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 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.

For more information about risks and side effects, ask your 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 chemotherapy and/or hormonal therapy will be more useful against cancer compared to the usual treatment, there is no proof of this yet. We do know that the information from this study will help doctors learn more about chemotherapy and/or hormonal therapy as a treatment for cancer. 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?

The Eastern Cooperative Oncology Group (ECOG) is conducting this study. ECOG is a cancer group that conducts studies for the National Cancer Institute. Your doctor is a member of ECOG or another group that is participating in this study. To help protect your privacy, ECOG has obtained a Confidentiality Certificate from the Department of Health and Human Services (DHHS).

With this Certificate, ECOG cannot be forced (for example, by court subpoena) to disclose information that may identify you in any federal, state or local civil, criminal, administrative, legislative or other proceedings. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes.

You should understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about you or your involvement in this research. Note, however, that if an insurer or employer learns about your participation and obtains your consent to receive research information, then ECOG

may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your privacy.

Finally, you should understand that your doctor and ECOG are not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others and the Certificate does not prevent the review of your research records under some circumstances by certain organizations for an internal program audit or evaluation. Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as:

- Eastern Cooperative Oncology Group
- National Cancer Institute
- Food and Drug Administration
- Other regulatory agencies and/or their designated representatives
- Drug manufacturers, and/or their representatives
- Central Laboratories
- Cancer Trials Support Unit (CTSU), a research group sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials

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. The docetaxel will be provided free of charge, when starting hormone therapy but will not be provided free of charge if your disease worsens, as this would be standard of care. 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.

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 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.

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 doctor about any questions or concerns you have about this study. Contact your 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 1-906-228-9440, ext. 3183

Please note: This section of the informed consent form is about additional research studies that are being done with people who are taking part in the main study. You may take part in these additional studies if you want to. You can still be a part of the main study even if you say 'no' to taking part in any of these additional studies.

You can say "yes" or "no" to each of the following studies. Please mark your choice for each study.

Quality of Life Study

We want to know your view of how your life has been affected by cancer and its treatment. This “Quality of life” study looks at how you are feeling physically and emotionally during your cancer treatment. It also looks at how you are able to carry out your day-to-day activities.

This information will help doctors better understand how patients feel during treatments and what effects the medicines are having. In the future, this information may help patients and doctors as they decide which medicines to use to treat cancer.

You will be asked to complete 5 questionnaires: one on your first visit, one at 3 months (week 12), one at 6 months (week 24), one at 9 months (week 36), and one at 12 months (week 48). Each questionnaire has 4 parts. It takes about 15 minutes to fill out each questionnaire.

If any questions make you feel uncomfortable, you may skip those questions and not give an answer.

If you decide to take part in this study, the only thing you will be asked to do is fill out the five questionnaires. You may change your mind about completing the questionnaires at any time.

Just like in the main study, we will do our best to make sure that your personal information will be kept private.

Please circle your answer.

I choose to take part in the Quality of Life Study. I agree to fill out the five Quality of Life Questionnaires.

YES

NO

SCIENTIFIC STUDIES

This study includes one or more laboratory tests that will analyze a small sample of blood and tissue. The tissue sample will be from your diagnostic biopsy, an additional biopsy will not be needed. Blood will be collected by inserting a needle into a vein and drawing 2 to 4 tablespoons of blood. This will be done before you begin treatment, 6 months into your treatment, and if your disease progresses. The tissue and blood will be sent to central laboratories, where researchers will perform tests in order to better understand prostate cancer. The results from these tests will not be sent to you or your doctor, and they will not be used in planning your care. These tests are only for research purposes.

Making Your Choice

Please read the sentence below and think about your choice. After reading the sentence, circle "Yes" or "No." *No matter what you decide to do, it will not affect your care.* You can participate in the treatment part of the study without participating in the research studies. If you have any questions, please talk to your doctor or nurse.

I agree to participate in the scientific laboratory research studies that are being done as part of this clinical trial.

Yes No

WILL ANY OF THE SAMPLES (E.G., TISSUE) TAKEN FROM ME BE USED FOR OTHER RESEARCH STUDIES?

About Using Tissue for Research

If you participate in the laboratory study associated with this protocol, you will have some blood and the biopsy material from your original diagnostic biopsy sent to central laboratories for analysis. The samples of blood and tissue are referred to as specimens.

We would like to keep some of the specimens that are left over for future research. If you agree, these specimens will be kept and may be used in research to learn more about cancer and other diseases. The specimens will be given only to researchers approved by the Eastern Cooperative Oncology Group (ECOG). Any research done on the specimens also must be approved by the researcher's Institutional Review Board.

Your specimens may be helpful for research, whether you do or do not have cancer. The research that may be done with your specimens will probably not help you. It might help people who have cancer and other diseases in the future.

Reports about the research done with your specimens will not be given to you or to your doctor. These reports will not be put into your health record. The research will not have an effect on your care.

Things to Think About

The choice to let us keep the leftover specimens for future research is up to you. No matter what you decide to do, it will not affect your care, and you may still take part in the Eastern Cooperative Oncology Group study.

If you decide now that your specimens 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 do not want us to use your specimens]. Then the specimens will no longer be used for research.

In the future, people who do research may need to know more about your health. When the Eastern Cooperative Oncology Group gives those reports about your health, it will not give them your name.

Sometimes specimens are used for genetic research (about disease that is passed on in families). Even if your specimens are used for this kind of research, the results will not be put into your health records.

Your specimens will be used only for research, and it will not be sold. You will not be paid for allowing your leftover specimens to be used in research, even though the research done with your specimens may help to develop new products in the future. Similarly, there will be no cost to you for any specimens collected and stored by the Eastern Cooperative Oncology Group.

It is possible that, at some time in the future, as part of deciding on which therapy to give you, a new test might become available that could be done on some of the tissue that is now thought of as “leftover.” This situation is unusual, but it could happen. In order to see that not all of this leftover tissue is used up, the Eastern Cooperative Oncology Group will take care to see that some of your cancer tissue is stored for 10 years so it is available if you or your doctors should need it.

This will depend upon the amount of leftover tissue that is submitted for this study. However, there may not be any leftover blood and tissue to store.

Benefits

The benefits of research using specimens include; learning more about what causes cancer and other diseases, how to prevent them, how to treat them, and how to cure them.

Risks

There are very few risks to you. The greatest risk is the release of information from your health records. The Eastern Cooperative Oncology Group will protect your records so that your name will be kept private. The chance that this information will be given to someone else is very small.

Making Your Choice

Please read each sentence below and think about your choice. After reading each sentence, circle "Yes" or "No." **No matter what you decide to do, it will not affect your care.** You can participate in the treatment part of the study without participating in all or part of the blood and tissue research studies. If you have any questions, please talk to your doctor or nurse.

<p>My specimens may be kept for use in research to learn about, prevent, treat, or cure cancer.</p> <p>Yes No</p>
<p>My specimens may be kept for use in research about other health problems (for example, causes of diabetes, Alzheimer's disease, and heart disease).</p> <p>Yes No</p>
<p>Someone from this institution may contact me in the future to ask me to take part in more research.</p> <p>Yes No</p>

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 doctor.

SIGNATURE

I have been given a copy of all 16 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 _____

IRB approved 12/10/2010
IRB approved 08/10/2011