

**MARQUETTE GENERAL HEALTH SYSTEM  
Regional Medical Center**

**CONSENT TO PARTICIPATE IN AN INVESTIGATIONAL STUDY**

**TITLE: SWOG S0226 - Phase III Randomized Trial of Anastrozole Versus Anastrozole and Fulvestrant as First Line Therapy for Post Menopausal Women with Metastatic Breast Cancer**

**INVESTIGATORS: Sheetal Acharya,MD  
Adnan Alkhalili,MD  
Mohammed Al-Nsour,MD  
Daniel Arnold,MD  
Gustavo Morel,MD  
Suresh Nukala,MD  
Irina Sachelarie,MD  
Aaron Scholnik, MD  
1414 W. Fair Avenue  
Marquette, MI 49855**

This is a clinical trial (a type of research study). Clinical trials include only patients who choose to take part. Please take your time to make your decision. Discuss it with your family and friends.

You are being asked to take part in this study because you have breast cancer that has spread to other parts of your body (metastasized).

**Why Is This Study Being Done?**

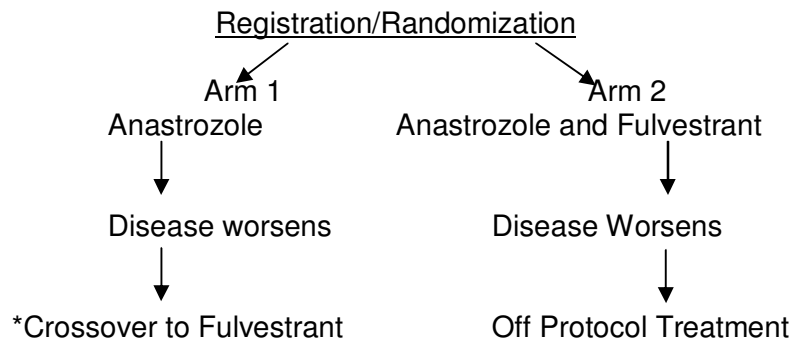
**The purpose of this study is to find out what effects (good or bad) the combination of hormonal agents anastrozole and fulvestrant have over anastrozole alone on you or your breast cancer. Both drugs anastrozole and fulvestrant are approved by the Food and Drug Administration for the treatment of metastatic breast cancer. However, it is the combination of the two drugs that is considered experimental.**

**As part of this study, researchers would also like to do laboratory testing on tissue samples and blood samples to find out as much as possible about breast cancer and how this treatment might affect the disease. They would also like to use the tissue and blood to find out about other cancers or other diseases. At the end of this form, you may choose to allow some excess tissue from your tumor and your blood to be kept and used for research purposes.**

**How Many People Will Take Part in the Study?**

In total, about 690 women will take part in this study.

## What Is Involved in the Study?



\*Recommended for certain patients.

NOTE: "Crossover" means to change treatment from anastrozole to fulvestrant.

You will be "randomized" into one of the two study groups described below. This means that you are put into a group by chance. It is like flipping a coin. Which group you are put into is done by a computer. Neither you nor the researcher will choose what group you will be in. You will have an equal chance of being placed in either group.

Some people will receive 1 mg of anastrozole by mouth every day. Others will receive 1 mg of anastrozole by mouth every day, and an initial dose of 500 mg of fulvestrant as a shot into a muscle (250 mg shot into each buttock) will be given. Then on Days 14 and 28 you will receive a single 250 mg shot into the buttock. Thereafter, you will receive 250 mg of fulvestrant as a single shot once every 28 days. This schedule will continue until the disease gets worse or the side effects are not acceptable.

You will have the choice to receive fulvestrant if your disease becomes worse and if you do not need other treatment right away.

Your doctor will see you for regular checkups.

If you take part in this study, you will have the following tests and procedures regardless of which group you are in:

Tests that are part of regular cancer care and may be done even if you do not join the study.

- Physical Exam
- Chest x-ray
- Blood Counts, tumor markers
- Scans

Standard tests being done because you are in this study

- Blood test for side effects
- Other exams for side effects

Exams that are being tested in this study

We encourage patients in each group to give blood to have measurements of drug levels done in order to assess how your body is metabolizing the drugs (called pharmacokinetic testing). We will only collect blood from fifty patients in each group (100 total).

If you agree to submit blood specimens for pharmacokinetic testing the following will be done:

If randomized to Arm 1: Three (3) tablespoons of blood will be drawn prior to starting treatment and at months 2, 4, 6, and 8 (prior to getting anastrozole).

If randomized to Arm 1 (with cross-over to fulvestrant): Three (3) tablespoons of blood will be drawn prior to starting treatment, at day 28 and at months 2, 4, 6, and 8 (prior to getting fulvestrant).

If randomized to Arm 2: Three (3) tablespoons of blood will be drawn prior to starting treatment, at day 14 and 28 and at months 2, 4, 6, and 8 (prior to getting fulvestrant). Prior to starting treatment and at months 2, 4, 6, and 8 an additional 10 mL of blood (approximately 2 teaspoons) will be drawn to determine estradiol levels.

Each time you visit your doctor, blood will be taken for routine tests. An extra 7 ml (approximately one teaspoon) will be drawn into another tube and sent to the Southwest Oncology Group serum bank for storage. These samples will be tested for new blood markers that might help us sort out who was more or less likely to gain from the treatment after the study is complete. Since these are investigational tests, neither you nor your doctor will be informed of the results, because we do not know whether they should or can be used to make treatment decisions (in fact, that is the reason to do the study). Also, they will not be studied until the entire study is over, which will be years from now.

No extra visits will be required for these studies.

Please see the additional consent form about the Southwest Oncology Group Tissue and Serum Bank at the end of this consent form ("Consent Form for the Use of Specimens in Research").

### **How Long Will I Be in the Study?**

We think you will be in the study until your disease gets worse or the side effects become too severe. Your disease status will be followed for up to four years.

The researcher may decide to take you off this study if your disease gets worse despite the treatment; the side effects of the treatment are too dangerous for you; new information about the treatment becomes available and this information suggests the treatment will be ineffective or unsafe for you. It is unlikely, but the study may be stopped early due to lack of drug supply or lack of funding.

## What Are the Risks of the Study?

While on the study you are at risk for the side effects described below. You should discuss these with the researcher and/or your regular doctor. There also may be other side effects that we cannot predict. Care will be taken during the treatment to make side effects less serious and uncomfortable. Many side effects go away shortly after the treatment is stopped, but in some cases side effects can be serious or long-lasting or permanent.

Below are side effects reported in studies comparing fulvestrant and anastrozole. These side effects may or may not have been related to fulvestrant or anastrozole.

### **Likely (these risks occur in 10%- 30% of the patients taking fulvestrant )**

Trouble breathing  
Cough  
Warmth or redness in the face, neck, arms, or upper chest (hot flashes)  
Headache or back pain  
Nausea, vomiting, constipation, diarrhea, or stomach pain  
Pain and/or swelling where the shot is given  
Tiredness or weakness  
Vaginal irritation  
Bone or abdominal pain

### **Less Likely (these risks occur in 5% - 9% of the patients taking fulvestrant)**

Chest Pain  
Fever, chills, sore throat, body aches  
Loss of appetite  
Rash, usually mild in nature  
Urinary tract infections, usually mild in nature  
Changes in body odor  
Lowered red blood cell count, which may cause tiredness and weakness  
Problems sleeping  
Fluid retention  
Sweating  
Weight gain  
Sore throat  
Dizziness  
Depression  
Feeling of numbness and tingling

### **Rare but serious (these risk occur in < 1% of patients taking fulvestrant but are considered serious)**

Abnormal blood clots in your arms or legs that may reach the lung  
Vaginal bleeding  
Muscle pain  
Lowered white blood cell count, which may increase risk of infection

The following are risks may or may not have been associated with anastrozole:

**Likely (these risks occurred in 10% - 30% of patients taking anastrozole)**

Nausea and/or vomiting  
Sore throat  
Hot flashes  
Weakness  
Joint pain  
Mood changes  
Rash  
Tiredness  
Bone loss

**Less Likely (these risks occurred in 5% - 10% of patients taking anastrozole)**

Diarrhea  
Trouble breathing  
Back pain  
Bone pain  
Constipation  
Cough  
Chest Pain  
Dizziness  
Flu syndrome  
Fever  
Headache  
Loss of appetite  
Stomach pain  
Numbness and tingling in hands and feet  
Fluid retention  
Sweating  
Urinary tract infections  
Muscle pain  
Increased blood pressure  
Increased liver function test  
Bone fractures  
Vaginal bleeding  
Decreased red blood cell count  
Difficulty sleeping  
Thinning hair  
Vaginal dryness  
Sleepiness  
Increased cholesterol  
Dry mouth

**Rare but Serious, (these risks occurred in < 1% of patients taking anastrozole but are considered serious)**

Abnormal blood clots that may reach the lung  
Skin reactions involving ulcers  
Whom can I call if I have questions or problems?

In the event that physical injury occurs as a result of this research, facilities for treatment of injury will be available; however, you will not automatically be provided with reimbursement for medical care or other compensation. For more information concerning the research and research-related risks or injuries, you can notify Dr. \_\_\_\_\_, or his/her associates, who may be reached by phoning the office at (906) 225-3922. During the evenings, weekends, or holidays you may phone Marquette General Health System at (906) 228-9440, and request to speak with the medical oncologist on call. You can also call the Patient Advocate at Marquette General Health System at (906) 228-9440, if you have any questions, comments, or concerns about the study or your rights as a research subject.

### **Are There Benefits to Taking Part in the Study?**

We cannot and do not guarantee you will benefit if you take part in this study. The treatment you receive may even be harmful. Your doctors feel that your taking part in this study will give you at least as good a chance as you might expect from other treatments. We hope the information learned from this study will benefit other patients with metastatic breast cancer in the future.

### **What Other Options Are There?**

Instead of being in this study, you have these options:

You may receive this hormone therapy or other chemotherapy for your cancer or you may choose no anti-cancer treatment at this time (with care to help you feel more comfortable). The drug trastuzumab (Herceptin<sup>®</sup>) may also be considered if your tumor cells are positive for the HER2 neu protein.

You can get treatment for metastatic breast cancer without being on this study. All of the treatment on this study may be available at this center or at other places.

Please talk to your regular doctor about these and other options.

### **What about Confidentiality?**

Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as: the National Cancer Institute or its authorized representatives, the Food and Drug Administration, AstraZeneca Pharmaceuticals, the Southwest Oncology Group, the Cancer Trials Support Unit (CTSU, a research group sponsored by the National Cancer Institute [NCI] to provide greater access to cancer trials and other cooperative groups participating on this study). If we publish the information we learn from this study in a medical journal, you will not be identified by name or in any other way.

For patients registered by another cooperative group, records of patient progress while on study will be kept in a confidential file at both the other cooperative group and the Southwest Oncology Group.

### **What Are the Costs?**

Taking part in this study may lead to added costs to you or your insurance company. Please ask about any expected added costs or insurance problems.

In the case of injury or illness resulting from this study, emergency medical treatment is available but will be provided at the usual charge. No funds have been set aside to compensate you in the event of injury. Although no funds have been set aside to compensate you for injury or illness related to the study treatment or procedures, you do not have to give up any of your legal rights for compensation by signing this paper.

You or your insurance company will be charged for continuing medical care and/or hospitalization.

You will receive no payment for taking part in this study.

You or your insurance company will have to pay for the administration of the drugs used in this study. Administration of the treatment will be charged in the usual way. AstraZeneca, will provide you with the anastrozole and/or fulvestrant at no cost to you while you are participating in this study. However, if you should need to take the study agent(s) much longer than is usual, it is possible that the free supply of study agent(s) given to you through the study could run out. If this happens, your study doctor will discuss with you how to obtain additional drug from the manufacturer and you may be asked to pay for it.

Medicare should be considered a health care provider. The parts of the research consisting of keeping research records will be paid by those organizing and conducting the research. The research requires that you receive certain standard medical tests and examinations. These standard tests and examinations will be charged in the usual way.

You may find a National Cancer Institute Guide: "Clinical Trials and Insurance Coverage – A Resource Guide" helpful in this regard. You may ask your doctor for a copy, or it is available on the worldwide web at <http://cancer.gov/clinicaltrials/insurance>.

### **INSTITUTIONAL FUNDING:**

Funds are provided from the study sponsor to Marquette General Hospital on a per patient basis to help with the institution's costs of participating in this study.

## **RIGHT TO WITHDRAW:**

Whether or not you take part in this study will not affect your future relations with your doctors or Marquette General Hospital. If you decide to take part, you are free to stop whenever you want to. You understand that you have the right to refuse to participate in this research study if you so desire without any fear of prejudice to additional treatment for yourself. In addition, you understand that you may refuse to continue on this study, at any time after the start of therapy, without fear of prejudice to additional treatment you may need. You recognize that you have received a copy of this consent form, and your signature indicates that you have volunteered to participate in the study having read the information provided to you.

A Data Safety and Monitoring Board, an independent group of experts, will be reviewing the data from this research throughout the study. We will tell you about important new information from this or other studies that may affect your health, welfare, or willingness to stay in this study.

## **WHOM DO I CALL IF I HAVE PROBLEMS OR QUESTIONS?**

In the event that physical injury occurs as a result of this research, facilities for treatment of injury will be available; however, you will not automatically be provided with reimbursement for medical care or other compensation. For more information concerning the research and research-related risks or injuries, you can notify Dr. \_\_\_\_\_, or his/her associates, who may be reached by phoning the office at (906) 225-3922. During the evenings, weekends, or holidays you may phone Marquette General Hospital at (906) 228-9440, and request to speak with the oncology physician on call. You can also call the Patient Advocate at Marquette General Hospital at (906) 228-9440, if you have any questions, comments, or concerns about the study or your rights as a research subject.

## **WHERE CAN I GET MORE INFORMATION?**

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

Visit the NCI's Web sites...

cancerTrials: comprehensive clinical trials information <http://cancertrials.nci.nih.gov>

CancerNet™: accurate cancer information.

You will get a copy of this form. You may also request a copy of the protocol (full study plan).

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

**Future Contact**

I agree to allow my study doctor, or someone approved by my study doctor, to contact me regarding future research involving my participation in this study.

**Yes**

**No**

**Pharmacokinetic Testing**

I agree to submit blood samples for the purposes of determining how my body metabolizes the drugs, fulvestrant and anastrozole.

**Yes**

**No**

**Genetic Testing**

We would also like to use your DNA (material inside cells that carry genetic information) to look at common forms of genes that may affect how the protocol treatment is being processed by your body and to understand how these genes may affect your response to protocol treatment. For this reason, we will be collecting one 10 mL tube of blood (approximately 2-3 tablespoons) prior to the initiation of protocol treatment. If you are willing to allow this specimen to be used for research purposes, please specify your consent below:

I agree to submit a blood specimen for genetic expression studies to study what role the protocol treatment is having on my disease.

**Yes**

**No**

**Your signature below means that you have freely agreed to participate in this investigational study.**

\_\_\_\_\_  
Patient's Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature of person conducting  
Informed consent discussion

\_\_\_\_\_  
Date

**I certify that the nature and purpose, the potential benefits, and possible risks associated with participation in this research study have been explained to the patient indicated, and that any questions about this information have been answered.**

\_\_\_\_\_  
Investigator's Signature

\_\_\_\_\_  
Date

**Your signature below means that you do not wish to participate in this investigational study.**

\_\_\_\_\_  
Patient's Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature of person conducting  
Informed consent discussion

\_\_\_\_\_  
Date

\_\_\_\_\_  
Investigator's Signature

\_\_\_\_\_  
Date

IRB approved: 2/8/06  
IRB to review Amend. #4 7/12/2006  
Revision #2 05/15/2008  
Revision #3 11/12/2008

Southwest Oncology Group Solid Tumor Tissue Bank  
University of Colorado HSC at Fitzsimons  
Department of Pathology  
RC-1 South, Room L18-5400-A  
12801 East 17<sup>th</sup> Avenue  
Aurora, CO 80045  
Phone: 303/724-3086

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.

### **Consent Form for Use of Specimens For Research**

#### **ABOUT USING SPECIMENS FOR RESEARCH**

You have had a biopsy (or surgery) to identify your cancer. Your doctor has removed some body tissue to do some tests. The results of these tests have been given to you by your doctor and will be used to plan your care.

We would like to keep some of the tissue that is left over for future research. If you agree, this tissue will be kept and may be used in research to learn more about cancer and other diseases. Additionally, please read the question and answer sheet (attached) called "How are Specimens Used for Research" to learn more about specimen research. Additionally we would like to study your blood samples to learn more about your cancer.

The research that may be done with your specimens probably will not help you. It might help people who have cancer and other diseases in the future.

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

#### **Things to Think About**

The choice to let us keep the left over specimens for future research is up to you. No matter what you decide to do, it will not affect your care.

If you decide now that your specimens can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your specimen. Then the specimen will no longer be used for research.

In the future, people who do research may need to know more about your health. When the Southwest Oncology Group gives them reports about your health, it will not give them your name, address, or phone number.

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

Your specimens will be used only for research and will not be sold. The research done with your specimens may help to develop new products in the future.

**Benefits**

The benefits of research using specimen 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 Southwest Oncology Group 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.

Please read each sentence below and think about your choice. After reading each sentence, check "Yes" or "No." **No matter what you decide to do, it will not affect your care.**

**VOLUNTARY CONSENT:**

You certify that you have read the preceding or it has been read to you and that you understand its contents. Any questions you have pertaining to the research or research related injuries have been and will be answered by Dr. \_\_\_\_\_ or his/her associates, who may be reached by phoning the office at (906) 225-3922. During evenings, weekends, or holidays you may phone Marquette General Hospital at (906) 228-9440, and request to speak with the medical oncologist on call. Any questions you have concerning your rights as a research subject will be answered by the Patient Advocate at Marquette General Hospital, who may be reached by phoning (906) 228-9440. You will be given a copy of this consent form.

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**1. My specimens may be kept for use in research to learn about, prevent, treat, or cure cancer.**

Yes \_\_\_\_\_ No \_\_\_\_\_

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**2. My specimens may be kept for use in research about other health problems (for example: causes of diabetes, Alzheimer's disease, or heart disease).**

Yes \_\_\_\_\_ No \_\_\_\_\_

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**3. Someone may contact me in the future to ask me to allow other uses of my specimens.**

Yes \_\_\_\_\_ No \_\_\_\_\_

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**If you decide to withdraw your specimens from a Southwest Oncology Group Specimen Repository in the future, a written withdrawal of consent should be submitted through your treating physician to the Southwest Oncology Group Operations Office. Please designate in the written withdrawal whether you would prefer to have the specimens destroyed or returned to the treating physician.**

Please sign your name here after you check your answers.

Participant \_\_\_\_\_ Date \_\_\_\_\_

### **How are Specimens Used for Research?**

#### **Where do specimens come from?**

A specimen may be from a blood sample or from bone marrow, skin, toenails or other body materials. People who are trained to handle specimens and protect donors' rights make sure that the highest standards of quality control are followed by the Southwest Oncology Group. Your doctor does not work for the Southwest Oncology Group, but has agreed to help collect specimens from many patients. Many doctors across the country are helping in the same way.

#### **Why do people do research with specimens?**

Research with specimens can help to find out more about what causes cancer, how to prevent it, how to treat it, and how to cure it. Research using specimens can also answer other health questions. Some of these include finding the causes of diabetes and heart disease, or finding genetic links to Alzheimer's.

#### **What type of research will be done with my specimen?**

Many different kinds of studies use specimens. Some researchers may develop new tests to find diseases. Others may develop new ways to treat or even cure diseases. In the future, some of the research may help to develop new products, such as tests and drugs. Some research looks at diseases that are passed on in families (called genetic research). Research done with your specimen may look for genetic causes and signs of disease.

#### **How do researchers get the specimen?**

Researchers from universities, hospitals, and other health organizations conduct research using specimens. They contact the Southwest Oncology Group and request samples for their studies. The Southwest Oncology Group reviews the way that these studies will be done, and decides if any of the samples can be used. The Southwest Oncology Group gets the specimen and information about you from your hospital, and sends the specimen samples and some information about you to the researcher. The Southwest Oncology Group will not send your name, address, phone number, social security number or any other identifying information to the researcher.

#### **Will I find out the results of the research using my specimen?**

You will not receive the results of research done with your specimen. This is because research can take a long time and must use specimen samples from many people

before results are known. Results from research using your specimen may not be ready for many years and will not affect your care right now, but they may be helpful to people like you in the future.

**Why do you need information from my health records?**

In order to do research with your specimen, researchers may need to know some things about you. (For example: Are you male or female? What is your race or ethnic group? How old are you? Have you ever smoked?) This helps researchers answer questions about diseases. The information that will be given to the researcher may include your age, sex, race, diagnosis, treatments and family history. This information is collected by your hospital from your health record and sent to the Southwest Oncology Group. If more information is needed, the Southwest Oncology Group will send it to the researcher.

**Will my name be attached to the records that are given to the researcher?**

No. Your name, address, phone number and anything else that could identify you will be removed before they go to the researcher. The researcher will not know who you are.

**How could the records be used in ways that might be harmful to me?**

Sometimes, health records have been used against patients and their families. For example, insurance companies may deny a patient insurance or employers may not hire someone with a certain illness (such as AIDS or cancer). The results of genetic research may not apply only to you, but to your family members too. For disease caused by gene changes, the information in one person's health record could be used against family members.

**How am I protected?**

The Southwest Oncology Group is in charge of making sure that information about you is kept private. The Southwest Oncology Group will take careful steps to prevent misuse of records. Your name, address, phone number and any other identifying information will be taken off anything associated with your specimen before it is given to the researcher. This would make it very difficult for any research results to be linked to you or your family. Also, people outside the research process will not have access to results about any one person which will help to protect your privacy.

**WHOM DO I CALL IF I HAVE PROBLEMS OR QUESTIONS?**

In the event that physical injury occurs as a result of this research, facilities for treatment of injury will be available; however, you will not automatically be provided with reimbursement for medical care or other compensation. For more information concerning the research and research-related risks or injuries, you can notify Dr. \_\_\_\_\_, or his/her associates, who may be reached by phoning the office at (906) 225-3922. During the evenings, weekends, or holidays you may phone Marquette General Hospital at (906) 228-9440, and request to speak with the oncology physician on call. You can also call the Patient Advocate at Marquette General Hospital at (906) 228-9440, if you have any questions, comments, or concerns about the study or your rights as a research subject.

