UCSF University of California San Francisco
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UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

CC#15754: Breast capsular contracture following post-mastectomy reconstruction in women treated with the leukotriene inhibitor zafirlukast: A Phase II Trial

This is a clinical trial, a type of research study. Your study doctors, [redacted] or one of their associates from the UCSF Helen Diller Family Comprehensive Cancer Center, 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 participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

You are being asked to take part in this study because you will be undergoing mastectomy with immediate tissue-expander reconstruction.

Why is this study being done?

The purpose of this study is to find out if the drug zafirlukast (Accolate™) is safe to use in post-mastectomy patients and if it has beneficial effects in reducing capsular contracture. A capsule around a breast implant is a naturally occurring tissue that often causes no problems. However, if that capsule *contracts* or thickens, it can squeeze your implant. This contracture is what will cause pain, shifting, distortion, and hardening of the reconstructed breast.

Zafirlukast is in a class of medications called leukotriene receptor antagonists. It works by blocking the action of certain natural substances that cause swelling and tightening of the airways. It is currently FDA approved to prevent asthma symptoms. However, it has not been approved by the US Food and Drug Administration (FDA) for the treatment of people with breast capsular contracture.

UCSF's Center for BRCA Research and the National Center of Excellence in Women's Health (NCOEWH) are providing funding to the investigator and UCSF to conduct the study.

How many people will take part in this study?

About 90 people who will be undergoing mastectomy with immediate tissue-expander reconstruction will take part in this study at UCSF. There will be two study groups. There will be 45 people in each group; one group will be followed with standard of care, and the other group will be given zafirlukast in addition to their regular care.

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What will happen if I take part and how long will I be in this research study?

If you give your consent to be in this study by signing this form, you will have tests and procedures (called "screening") done. These are done to reduce the risks of taking part in this study and to make sure it is okay for you to be in the study.

It is possible that after these tests are reviewed, you will not be able to be in the study. There may be other reasons why you cannot be in this study. These reasons will be discussed with you by your study doctor or the clinic staff.

Before you begin the main part of the study:

You will need to have the following exams, tests or procedures within 28 days prior to the day of your surgery to find out if you can be in the main part of 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 study doctor. This clinic visit may take approximately 2 hours.

- **Medical history**
- **Physical exam:** Including your height and weight, and vital signs
- **Blood draw**: Approximately 1 tablespoon of blood will be drawn for:
    - Routine safety tests
- **Pregnancy test**: A blood or urine pregnancy test will be performed if you are of child-bearing age.
- **Review of your medications** (both prescription and over-the-counter) and side effects

During the main part of the study:

<u>You will be randomized into one of two groups:</u>

Group 1: Treatment with zafirlukast and standard of care
Group 2: Standard of care alone

Participants assigned to Group 1 will begin treatment with zafirlukast on post-operative day one (up to day 4) following placement of tissue expander(s), after you are determined safe from a surgical recovery standpoint. If you are in Group 1, you will take zafirlukast twice per day until you have completed expansion of the tissue expander. Your last dose of zafirlukast will be administered the day prior to expander implant exchange.

You should only take the study treatment as instructed and do nothing else with it. Each dose should be taken ***1 hour before*** a meal or ***2 hours after*** a meal with a large glass of water.

If the screening exams, tests and procedures show that you can be in the main part of the study, and you choose to take part, then you will need the following tests and procedures. The clinic visits may take about 1 hour.

Day 8-21 (week 2)

- **Physical exam** including your height and weight, and vital signs
- **Blood draw:** Approximately 1 tablespoon of blood will be drawn for:
  - Routine safety tests
- **Review of your medications** (both prescription and over-the-counter) and side effects

Day 28-42 (week 5)

- **Physical exam** including your height and weight, and vital signs
- **Blood draw:** Approximately 2 to 3 tablespoons of blood will be drawn for:
  - Routine safety tests
  - Liver function tests (if you are in Group 1)
- **Review of your medications** (both prescription and over-the-counter) and side effects

Day 70-84 (week 11)

- **Physical exam** including your height and weight, and vital signs
- **Blood draw:** Approximately 1 tablespoon of blood will be drawn for:
  - Routine safety tests
- **Review of your medications** (both prescription and over-the-counter) and side effects

Day 112-126 (week 17) (*If needed)*

- **Physical exam** including your height and weight, and vital signs
- **Blood draw**: Approximately 1 tablespoon of blood will be drawn for:
  - Routine safety tests
- **Review of your medications** (both prescription and over-the-counter) and side effects

Expander Implant Exchange

- Tissue collection of capsule (performed at the time of expander-implant exchange): As part of this study, we will obtain a small piece of tissue from the capsule during your surgery. This will be done during implant exchange. The tissue collected is used to us determine if zafirlukast can reduce the thickness and scarring of the capsule tissue compared to standard of care.

End of Treatment

- **Medical history**
- **Physical exam** including your height and weight, and vital signs
- **Blood draw:** Approximately 2 to 3 tablespoons of blood will be drawn for:
  - Routine safety tests
  - Liver function tests (if you are in Group 1)
- **Review of your medications** (both prescription and over-the-counter) and side effects

Follow-up Visits

- **Physical exam** including your height and weight, and vital signs

You will be followed for two years after reconstruction. After implant exchange, we would like to see you every 2 weeks for the first month, then every month for the next 4 months, and then every 6 months for the remainder of the two years. If you stop receiving treatment early, then we would like to follow you as per routine care, which is monthly for the first six months and then every six months for a total of two years.

Study location: All study procedures will be done at the UCSF Cancer Center.

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How long will I be in the study?

For participants in group 1 receiving zafirlukast, you will begin treatment with zafirlukast on post-operative day one (up to day 4) following placement of the tissue expander(s), until you have completed expansion. For both groups, after you have had your expander fill, the study doctor will ask you to visit the office for an End of Treatment visit approximately 14 days after surgery. In addition, your study doctor or staff will follow-up with you for 2 years after your reconstruction. If you do not want the study doctor or staff to contact you, you will need to withdraw your consent from this follow-up.

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. He or she will tell you how to stop your participation safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from zafirlukast 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 zafirlukast. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death. You should talk to your study doctor about any side effects you experience while taking part in the study.

Risks and side effects related to zafirlukast include those which are:

Common (>10%)

- Headache

Less common (1-10%)

- Infection
- Nausea
- Diarrhea
- Pain – general pain, abdominal pain, back pain
- Physical weakness or lack of energy (Asthenia)
- Dizziness
- Muscle pain (Myalgia)
- Fever
- Vomiting
- Increased enzymes (ALT) in the liver, which may indicate the liver is not working properly
- Indigestion (Dyspepsia)

In rare cases, the following side-effects have also been seen in patients on zafirlukast:

- High levels of white blood cells in the blood and lungs
- Inflammation of the blood vessels
- Difficulty sleeping
- Depression
- Rash and/or swelling of the skin
- Bleeding
- Bruising
- Swelling of the arms and/or legs
- Painful joints
- Itchy skin

Risks related to study procedures

- **Blood drawing (venipuncture) risks:** Drawing blood may cause temporary discomfort from the needle stick, bruising, infection, and fainting.

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- **Tissue collection of capsule risks:** The capsule around the tissue expander is usually removed at the time of expander-implant exchange, so there are no separate risks to this portion of the study. However, the surgery for expander-implant exchange does have the general surgical risks, including pain, bleeding, and infection. We check your laboratory values before surgery to make sure that the procedure is as safe as possible and to minimize your chance of having a complication. Other potential risks will be described to you and discussed with your surgeons who conduct these operations.

- **Reproductive risks:** You should not become pregnant while on this study because the drugs in this study may affect an unborn baby. Women should not breastfeed a baby while on this study. It is important to understand that you may need to use birth control while on this study. Check with you 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 become pregnant while on this study, you should inform the study doctor immediately.

- **Randomization risks:** You will be assigned to a treatment program by chance, and the treatment you receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments.

- **Unknown Risks:** The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

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 zafirlukast will reduce capsular contracture compared to the usual treatment, there is no proof of this. We do know that the information from this study will help doctors learn more about zafirlukast as a treatment for capsular contracture. 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.

Please talk to your doctor about your choices before deciding if you will take part in this study.

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How will information about me be kept confidential?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. Some information from your medical records will be collected and used for this study. If you do not have a UCSF medical record, one will be created for you. Your signed consent form and some of your research tests will be added to your UCSF medical record. Therefore, people involved with your future care and insurance may become aware of your participation and of any information added to your medical record as a result of your participation. Study tests that are performed by research labs, and information gathered directly from you by the researchers will be part of your research records but will not be added to your medical record. 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:

- The University of California
- The National Cancer Institute (NCI) and other government agencies, e.g., the Food and Drug Administration (FDA), involved in keeping research safe for people.

What are the costs of taking part in this study?

UCSF is supplying zafirlukast at no cost to you.

Two types of procedures will be done during this study. Some are part of your standard medical care and others are only for research. You or your insurer will be billed for the standard medical care. You will be responsible for your co-pays, deductibles, and any other charges that your insurer will not pay. Any procedures done only for research will not be charged to you or your insurer. There is a possibility that your insurer may not cover standard medical care costs because you are in a research study or because you are receiving medical services out of network.

Before you agree to be in this study, you may want to contact your healthcare payer/insurer to see if your plan will cover the costs required as part of your participation. You may request more information about the costs of participating in this study and discuss this with the study team. If you have any questions, your doctor and the study team will be able to provide you with answers.

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.

Will I be paid for taking part in this study?

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

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

It is important that you tell your study doctors, [redacted]. or Pamela Munster, M.D., if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call them [redacted].

Treatment and Compensation for Injury: If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California or the study sponsor, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at [redacted].

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, concerns, or complaints you have about this study. Contact your study doctor [redacted] or Pamela Munster, M.D. [redacted].

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the Office of the Committee on Human Research at [redacted].

ClinicalTrials.gov is a website that provides information about clinical trials. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

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CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

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If you wish to participate in this study, you should sign below.

Date	Participant's Signature for Consent
Date	Person Obtaining Consent
Date	Witness – Only required if the participant is a non-English speaker