

CTSU C70604

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Sponsored and Funded by the National Cancer Institute

CONSENT FORM

CTSU C70604: A Randomized, Phase III Study of Standard Dosing versus Longer Dosing Interval of Zoledronic Acid in Metastatic Cancer

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CTSU C70604

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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 breast cancer, prostate cancer or multiple myeloma and are at risk for problems with your bones. These problems include pain, fractures (broken bones), or the need for radiation therapy or surgery to bone.

Why Is This Study Being Done?

The purpose of this study is to compare the effects (good, bad or no difference) of less frequent treatment (every 12 weeks) with zoledronic acid (Zometa) compared to standard treatment (every 4 weeks) with zoledronic acid.

We know that treatment with zoledronic acid decreases the risk of certain bone related complications in people with breast cancer, prostate cancer or multiple myeloma AFTER the cancer has spread to the bones and continues to grow even with standard anti-cancer therapy. This research is being done because we do not know whether giving zoledronic acid less frequently will be as good as the standard dosing at preventing bone complications due to cancer. The research also hopes to find out whether less frequent dosing (every 12 weeks) of zoledronic acid is safer than more frequent dosing (every 4 weeks).

How Many People Will Take Part in the Study?

About 1540 people will take part in this study.

What Is Involved in the 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 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.

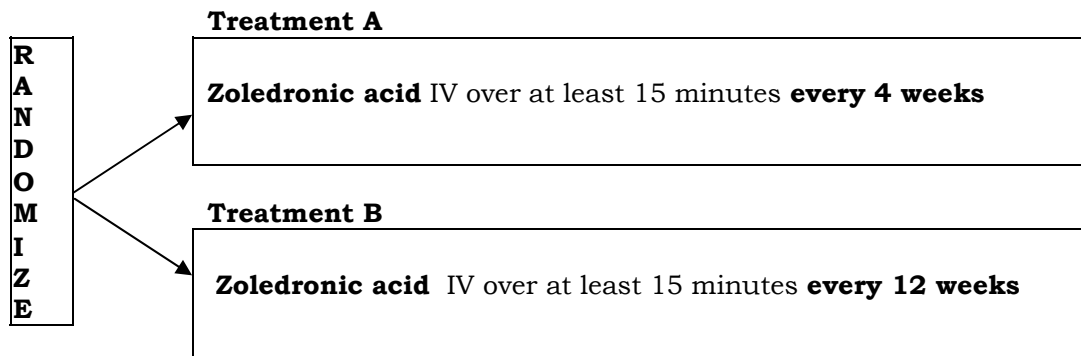
- A complete history and physical exam
- Blood tests
- Bone Scan
- Pregnancy test

In addition, you will be asked to answer a few questions about your dental history and complete a short questionnaire about any pain you may be feeling.

On rare occasions, patients treated with zoledronic acid have developed a serious dental problem (see below). It is recommended, but not required, that you see a dentist before starting treatment with zoledronic acid.

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 be “randomized” into one of the two study groups described below. Randomization means that you are put into a group by chance. A computer program will place you in one of the study groups. Neither you nor your doctor can choose which group you will be in. You will have an equal chance of being put into either of the two groups.



Treatment A

Patients randomized to Treatment A will receive zoledronic acid by intravenous infusion (IV) over 15 minutes or more once every 4 weeks for 2 years. This is done through a needle placed in a vein in your arm.

Treatment B

Patients randomized to Group B will receive zoledronic acid by intravenous infusion (IV) over 15 minutes or more once every 12 weeks for 2 years. This is done through a needle placed in a vein in your arm.

Daily calcium and vitamin D are recommended to maintain strong bones. You will be asked to take supplemental calcium (500 mg daily) and a multivitamin containing 400 IU vitamin D daily. You will be asked to take the calcium and vitamin D supplements with food. There are many preparations of calcium and vitamin D available without a prescription. You may choose one or discuss with your doctor which preparation would be best for you.

Tests and Procedures

If you take part in this study, you will have the following tests and procedures, which are part of regular cancer care and may be done even if you do not join the study.

- Blood tests every 4 weeks to measure kidney and liver functioning

If you participate in this study, some of these procedures may be done more frequently than if you were not taking part in this research study.

In addition, every 4 weeks we will ask you to answer the few questions about your dental history and to continue to complete the short questionnaire about any pain you may be feeling.

How Long Will I be in the Study?

You will be asked to take zoledronic acid for 2 years. The study doctor will ask you to visit the office every 4 weeks for the tests and questionnaires listed above for 2 years after you began participation in the study. We will ask you to continue to answer the questions about your dental history and complete the pain questionnaire every 4 weeks for 2 years whether or not you continue to take zoledronic acid.

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 safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the zoledronic acid 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 zoledronic acid. In some cases, side effects can be serious, long lasting, or may never go away. 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 zoledronic acid include those which are:

LIKELY:

- Fever
- Fatigue (tiredness)
- Anorexia or loss of appetite
- Nausea, vomiting, constipation, and /or abdominal pain
- Low levels of calcium in the blood, which may cause muscle cramps
- Flu-like symptoms including fever, chills, and joint and muscle aches, which are generally seen after the first infusion of zoledronic acid

LESS LIKELY:

- Headaches
- Insomnia
- Anxiety
- Stomach irritation
- Abnormal kidney function tests
- Diarrhea
- Tingling in the fingers and toes
- Bone, back, muscle, and joint pain. In some cases, this pain could be severe and could interfere with your going about your normal activities. You should tell your doctor if you have any new bone or joint or muscle pain.
- Allergic reactions, which include itching, flushing, rash, and shortness of breath
- Low levels of potassium, magnesium, and/or phosphate in the blood. In almost all cases, you would not experience symptoms from these effects. If these levels fall to extremely low levels, possible side effects could include muscle twitching, muscle weakness, and abnormal heart rhythm.
- A reaction at the injection site, which might include pain, redness, tenderness, swelling, and/or bruising.

RARE BUT SERIOUS

- Kidney failure
- Severe allergic reactions, which could include the inability to breathe and dangerously low blood pressure, which could be fatal
- Permanent damage to the jawbone (osteonecrosis of the jaw) that may be painful and might require surgery to remove the damaged area. This might be more likely to happen in patients who have certain dental procedures. If you see a dentist, you should inform him or her that you are receiving zoledronic acid.

Risks of Calcium and Vitamin D (Both Treatment Groups)

LIKELY:

- Constipation

LESS LIKELY:

- Headaches
- Kidney stones
- Stomach irritation
- High levels of calcium in the blood
- Nausea, vomiting
- Diarrhea

Other medications You should discuss all of your medications with your healthcare provider caring for you because certain drugs may increase the risk of developing side effects from zoledronic acid.

Unanticipated side effects may occur which have not been reported. If you have any unusual symptoms, report them immediately to your physician.

Reproductive risks: Because the drugs in this study may affect an unborn baby, you should not become pregnant or father a baby while on this study. Women should not breastfeed a baby while on this study. It is important you understand that you need to use birth regulation (highly effective: abstinence, IUD, birth control pills, tubal ligation or partner's vasectomy and less effective: condom, diaphragm or cervical cap) while on this study. Check with your study doctor about what kind of birth regulation (regulation highly effective: abstinence, IUD, birth control pills, tubal ligation or partner's vasectomy and less effective: condom, diaphragm or cervical cap) methods to use and how long to use them. For more information about risks and side effects, ask the study doctor the number listed on the cover page.

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 zoledronic acid taken every 3 months will be as effective as when it is taken every month, there is no proof of this yet. We do know that the information from this study will help doctors learn more about zoledronic to prevent skeletal related events. This information could help future cancer patients.

What Other Options Are There?

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

- You may choose to have treatment with zoledronic acid on a monthly schedule, which is considered standard treatment.
- You may choose not to receive treatment with zoledronic acid.
- You may choose another research study.

Please talk to your health care providers caring for you about these and other options.

What about Confidentiality?

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:

- The Cancer and Leukemia Group B (CALGB)
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people
- the Cancer Trials Support Unit (CTSU), a service sponsored by the NCI to provide greater access to cancer trials
- Novartis Pharmaceuticals

It may be necessary to contact you at a future date regarding new information about the treatment you have received. For this reason, we ask that you notify the institution where you received treatment on this study of any changes in address. If you move, please provide your new address to the following person:

(Karyn Hart, RHIT, CCRP
Program Coordinator
Northwest CCOP
315 Martin Luther King Jr., Way
Tacoma, WA 98405
(253) 403-1461

What Are the Costs?

You or your insurance company will be billed for the cost of zoledronic acid as well as for the blood tests that are part of the standard of care for receiving zoledronic acid.

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 him/her at the number listed on the cover page.

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.

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 the new information from this or other studies that may affect your health, welfare, or willingness to stay in this study.

Related Studies (optional participation):

In addition to the treatment study, the study doctor would also like to collect additional samples of your blood. We ask that you give approval for these tests to be performed using these samples.

Approximately 2 additional teaspoons of blood would be collected at the beginning of the study and every 12 weeks after that for up to 2 years when your other tests are done. The blood will be sent to a central laboratory for analysis.

These tests may provide additional information that will be helpful in understanding zoledronic acid's effect on skeletal related events. But, it is unlikely that what we learn from these studies will have a direct benefit to you. The information learned from these studies may benefit other patients in the future.

The results of these research studies will not be provided to you or your doctor. They will not be put in your health record, nor will the results have any effect on your treatment. In addition, some of the blood may be used to establish products to be patented or licensed. There are no plans to provide financial compensation to you if this occurs.

The greatest risk to you is the release of information from your health records. Blood samples will be stored at a CALGB laboratory. Your blood sample will not be stored with your name on it. Instead, it will be labeled with a special CALGB identification number. The only location where your name and special identification number will be stored together is at the CALGB Statistical Center. The greatest effort will be made to see that all personal information that can identify you is kept under conditions that protect your privacy. The results from these studies may be published, but individual patients will not be identified in these publications.

There will be no charge to you for participating in these related research studies.

The choice to participate in this study is entirely up to you. No matter what you decide to do, it will not affect your care. If you decide now that your blood can be used for research, you can change your mind at any time. Just let your doctor know that you do not want us to use your blood. Then any blood that remains will no longer be used for research.

Genetic studies on blood cells:

The researchers would like to investigate whether substances in your blood are related to the way that your body responds (or doesn't respond) to the zoledronic acid. These markers are inherited through your family, and could be passed to your children. These are also called genetic studies.

Your blood will be used to learn how certain genes influence the effectiveness and side effects of zoledronic acid. In order to study the genes the DNA must be removed from your blood sample. DNA is the substance that makes up your genes. Genes are the units of inheritance that are passed down from generation to generation. They are responsible for eye color, hair color, blood type, and hundreds of other traits.

There are specific risks associated with genetic studies. Genetic research may find medical conditions that affect you and your blood relatives since it looks at inherited traits. While your genes are unique to you, you share some of them with your blood relatives. It is possible that genetic research may find potential health concerns for you or your family. While this situation is rare, information could be misused by employers, insurance companies, and others. Your privacy and confidentiality will be protected to the fullest extent possible.

To help you make your decision, additional information about participation in genetic studies is included at the end of this consent form. This information identifies how your personal information will be protected by the Cancer and Leukemia Group B and its researchers.

Blood taken for these studies will be done only once at the time you enter the study. About 1 tablespoon of blood would be taken.

2) I agree that my blood may be used for the genetic research studies described above.

_____ Yes _____ No Initials _____

Future Studies (Optional participation):

The study doctors would also like to store any portion of the blood that is not used up by the related study described above. These samples may be stored indefinitely. You can still take part in the treatment study, and the research study described above without giving your consent for your samples to be stored.

It is not possible for you or the CALGB to know what studies of cancer may be appropriate in the future. We ask that you give permission in advance for other studies to be performed using the blood without being re-contacted to give permission for each test.

3. My specimen may be kept for future unknown use in research to learn about, prevent, treat, or cure cancer. _____ Yes _____ No Participant _____ Date _____
4. My blood may be kept for research about other health problems (for example: causes of diabetes, Alzheimers disease and heart disease). _____ Yes _____ No Participant _____ Date _____
5. My doctor or someone from CALGB may contact me in the future to ask me to take part in more research. _____ Yes _____ No Participant _____ Date _____

Whom Do I Call if I Have Questions or Problems?

For questions about the study or a research-related injury, contact the study doctor that is listed on the cover page.

For questions about your rights as a research participant, contact the MultiCare Health System Institutional Review Board (which is a group of people who review the research to protect your rights) at 253-403-3877.

You may also call the Project Office of the NCI Central Institutional Review Board (CIRB) at 888-657-3711 (from the continental US only)

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 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.

Patient's name (printed or typed)

Patient's Signature Date

Physician name (printed or typed)

Physician Signature Date

Signature of person conducting the
Informed consent discussion

Date

Safeguards of Confidentiality in Studies Involving Genes (genetic studies):

It is possible to use blood samples to study many different kinds of genes. The Cancer and Leukemia Group B recognizes this possibility and will take the following steps to protect your privacy and to protect you from having your sample tested for any genetic changes not directly related to cancer:

- Blood samples will be stored at a Cancer and Leukemia Group B laboratory. The Cancer and Leukemia Group B Statistical Center will perform all analyses of data and store all study results. Your blood sample will not be stored with your name on it. Instead, it will be labeled with a special Cancer and Leukemia Group B identification number. The only location where your name and special identification number will be stored together is at the Cancer and Leukemia Group B Statistical Center. The greatest effort will be made to see that all personal information that can identify you is kept under conditions that protect your privacy.
- Information about your participation in this study and results of any tests performed on your sample will be kept only at the Cancer and Leukemia Group B Statistical Center at Duke University. This information will not be made available to your doctors or to individual researchers at Cancer and Leukemia Group B. Test results from this study will not be put in your medical records. All study information, including test results, is stored under conditions that limit access in order to protect the privacy of the people participating in this study.
- Your blood will be used only for the study of genes involved in cancer.
- There are no absolute legal protections against discrimination on the basis of genetic information. Instances are known in which a patient has been required to provide genetic information before applying for health insurance and/or a job. Since neither you nor your physician will be notified of the results of this test, it is unlikely that any discrimination could take place.

The same precautions to protect your privacy will be in place for such future studies. Future investigators will receive blood samples with the special Cancer and Leukemia Group B identification number only, and your blood sample will not be identified with your name. These future investigators must apply to the Cancer and Leukemia Group B and have their research project reviewed and approved by the Cancer and Leukemia Group B.

If you decide now to give a sample of blood and then change your mind at any time about participating in the study, just contact your institution and let them know that you do not want the researchers to use your sample. The results from these studies may be published, but individual patients will not be identified in the publications.

Authorization (Permission) to Use or Disclose (Release) Identifiable Health Information for Research

Participant's Name: _____

Birth Date: _____

1. What is the purpose of this form?

The Northwest CCOP is an organization that does research to learn about the causes of cancer, and how to prevent and treat cancer. Researchers would like to use your health information for research. This information may include data that identifies you. Please carefully review the information below. If you agree that researchers can use your personal health information, you must sign and date this form to give them your permission.

2. What personal health information do the researchers want to use?

The researchers want to copy and use the portions of your medical record that they will need for their research. If you enter a Northwest CCOP research study, information that will be used and/or released may include the following:

- the history and diagnosis of your disease;
- specific information about the treatments you received, including previous treatment(s) you may have had;
- information about other medical conditions that may affect your treatment;
- medical data, including laboratory test results, tumor measurements, CT scans, MRIs, x-rays, and pathology results;
- information on side effects (adverse events) you may experience, and how these were treated;
- long-term information about your general health status and the status of your disease;
- data that may be related to tissue and/or blood samples that may be collected from you; and
- numbers or codes that will identify you, such as your social security number and medical record number.

You may request a blank copy of the Northwest CCOP data forms from the study doctor or his/her research staff to learn what information will be shared.

3. Why do the researchers want my personal health information?

The Northwest CCOP will collect your health information and share it with the Cancer and Leukemia Group (CALGB) Biostatistical Center and the CALGB Operations Center if you enter a cooperative group research study. The CALGB centers will use your information in their cancer research study. CTSU C70604: A Randomized, Phase III Study of Standard Dosing versus Longer Dosing Interval of Zoledronic Acid in Metastatic Cancer

4. Who will be able to use my personal health information?

The Northwest CCOP will use your health information for research. As part of this research, they may give your information to the following groups taking part in the research. The Northwest CCOP may also permit these groups to come in to review your original records that are kept by the Northwest CCOP so that they can monitor their research study.

- the CALGB Operations Center;
- the CALGB Biostatistical Center;
- the Cancer Trials Support Unit (CTSU), a research group sponsored by the National Cancer Institute that supports the research of the CALGB;
- Public Health agencies and other government agencies (including non-U.S.) as authorized or required by law;
- other people or organizations assisting with CALGB research efforts (this may include **Pharmaceutical Company(ies) (or designee[s]) and any subcontractors**), the company(ies) sponsoring the research); and
- central laboratories, central review centers, and central reviewers. The central laboratories and review agencies may also give your health information to those groups listed in the five bullets above.

4. How will information about me be kept private?

The CALGB will keep all patient information private to the extent possible, even though the CALGB is not required to follow the federal privacy laws. Only researchers working with the CALGB will have access to your information. The CALGB will not release personal health information about you to others except as authorized or required by law. However, once your information is given to other organizations that are not required to follow federal privacy laws, we cannot assure that the information will remain protected.

6. What happens if I do not sign this permission form?

If you do not sign this permission form, you will not be able to take part in the research study for which you are being considered.

7. If I sign this form, will I automatically be entered into the research study?

No, you cannot be entered into any research study without further discussion and separate consent. After discussion, you may decide to take part in the research study. At that time, you will be asked to sign a specific research consent form.

8. What happens if I want to withdraw my permission?

You can change your mind at any time and withdraw your permission to allow your personal health information to be used in the research. If this happens, you must withdraw your permission in writing. Beginning on the date you withdraw your permission, no new personal health information will be used for research. However, researchers may continue to use the health information that was provided before you withdrew your permission.

If you sign this form and enter the research study, but later change your mind and withdraw your permission, you will be removed from the research study at that time.

To withdraw your permission, please contact the person below. He/she will make sure your written request to withdraw your permission is processed correctly.

Karyn Hart, RHIT, CCRP
Program Coordinator
Northwest CCOP
315 Martin Luther King Jr., Way
Tacoma, WA 98405
(253) 403-1461

9. How long will this permission last?

If you agree by signing this form that researchers can use your personal health information, this permission has no expiration date. However, as stated above, you can change your mind and withdraw your permission at any time.

10. What are my rights regarding access to my personal health information?

You have the right to refuse to sign this permission form. You have the right to review and/or copy records of your personal health information kept by the Northwest CCOP. You do not have the right to review and/or copy records kept by the CALGB or other researchers associated with the research study.

Signatures

I agree that my personal health information may be used for the research purposes described in this form.

Patient's name (printed or typed)

Patient's Signature Date

Physician name (printed or typed)

Physician Signature Date

Signature of person conducting the
Informed consent discussion

Date