

**Department of Veterans Affairs
Research Consent Form**

VA AAHS Research IRB
Approved 12/09/2010
Expires 6/14/2011



Title of Study: A Phase I/II Clinical Trial of intravenous (IV) Calcitriol with fixed dose of Cisplatin and Docetaxel in Advanced Non-Small Cell Lung Cancer.

Principal Investigator: Nithya Ramnath

VAMC: VA Ann Arbor
Healthcare System

PURPOSE OF RESEARCH STUDY:

This is a research study and participation in this study is voluntary. This investigational/research study is being done by the doctors at the Roswell Park Cancer Institute, Buffalo, NY, at the University of Michigan Comprehensive Cancer Center, St. Joseph Mercy Hospital, Ann Arbor, MI and at the Veterans Administration Medical Center, Ann Arbor, MI. The purpose of this research study is to determine the safety of the combination of calcitriol with a standard platinum-based chemotherapy regimen in patients with advanced non-small cell lung cancer. The safety of this treatment will be determined by establishing a maximum tolerated dose and dose-limiting toxicities of calcitriol administered by intravenous infusion.

Calcitriol ("vitamin D") is a vitamin that appears to slow the growth of most cancers by binding to specific receptor sites in the cancer cells as well as blood vessels in these tumors and slowing their growth. In combination with platinum based chemotherapy, calcitriol has led to higher cancer cell kill rates as well in animals. Presently calcitriol is not approved by the Food and Drug Administration (FDA) for the treatment of NSCLC. The use of this drug in advanced lung cancer is investigational. Calcitriol is presently approved by the Food and Drug Administration (FDA) for the treatment of bone disease which occurs in individuals with kidney failure. However, it is important to note that calcitriol has already been studied in other human cancers such as prostate cancer and may have a survival benefit in that disease. Calcitriol (in various forms, intravenous (IV), subcutaneous, oral), in doses not approved by the FDA, has been administered to over 500 humans with very few side effects. At least one study in 32 patients used I.V. calcitriol in high doses weekly. We propose to use the IV formulation of calcitriol in combination with standard chemotherapy in patients with advanced NSCLC, in this study.

DESCRIPTION:

There are 2 phases of the study; enrollment into phase II will occur only after the phase I study is completed. In the Phase I part of the study, we will test the safety of calcitriol in conjunction with standard chemotherapy. In addition, the goal is to see to test the safety of calcitriol in combination with standard chemotherapy in Non-Small Cell Lung Cancer. In this portion of the study, we are testing increasing doses of vitamin D in combination with standard chemotherapy Dose levels 30 and 45mcg/m² of vitamin D have been completed. The 60mcg/m² dose level is enrolling patients. If no toxicity is noted at this level, you will be assigned to the next dose level (80 mcg/m² or higher); if there are no side effects, you will continue at that dose (along with chemotherapy) for up to 6 courses. You will receive the same constant dose of calcitriol during your participation on the study. We expect to enroll about 18 patients to the phase I study.

In the Phase II part of the study, we will find out the response your cancer has to the combination of a fixed dose of vitamin D (determined from the phase I study) with standard chemotherapy. We will record the effects (good and bad) of this regimen. The experimental part is the calcitriol administration. It is expected that about 39 patients are required for the phase II part of the study. This study will be open at 4 cancer centers including the VAMC. If you choose to participate, the duration will equal the period of treatment (range from 3 weeks to 6 months) until the end of the study when all participants have enrolled and followed-up. The range is given to account for factors that may not allow you to continue for the duration of the study: example due to side effects

RESEARCH SUBJECT IDENTIFICATION: (Required information)

				/ /
Last Name	First Name	Mid. Init.	Last-4 SSN	Date (mm/dd/yy)

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or lack of efficacy, requiring you to go onto other therapies.

Patients with advanced NSCLC (lung cancer that has spread beyond the lung) are eligible to participate in this study. **Pregnant subjects will not be included in this study.** The experimental part in both phases is the administration of calcitriol. Calcitriol is given just prior to standard chemotherapy every 21 days (1 cycle) for up to 6 cycles. The calcitriol injection is given over 60 minutes; the standard chemotherapy will take about 7 hours in the infusion area of the Oncology Clinic.

You will have approximately 30 mL (2 tablespoons) of blood drawn at your screening visit. This blood will be used to test the level of certain components of your blood to ensure you are eligible to participate in this study. This blood will also be used to perform a genetic test for a gene called CYP24. Sometimes this gene can affect your body's ability to use calcitriol. This test needs to be done at a central lab for the study, so the genetic sample will be sent out for analysis. Your sample will not be used for any other genetic testing.

All samples will be completely de-identified for analysis. There will be no use of actual patient names; all patients will be assigned an alpha-numeric code. Additionally, the samples will be destroyed at the end of the study so there is no chance they could be used in any future testing outside of the tests to which you have consented.

During each cycle, an additional blood sample (about 5 ml or 1 teaspoon) to monitor unusual or severe toxicity may also be drawn along with your routine laboratory tests. This will be used to determine how your body handles and eliminates calcitriol.

For the first cycle on the trial you will receive calcitriol on one day and the chemotherapy the next day. Before and after the dose of calcitriol, blood samples will be drawn at 4 fixed time points to look for levels of calcitriol in your blood. We will draw approximately 1.5 teaspoons (about 7 ml) at each time point for a total of approximately 6 teaspoons (28 ml). We want to study how the blood levels of calcitriol may compare with changes in the CYP24 gene that affect your body's ability to use calcitriol. For the rest of the cycles in the study you will receive the calcitriol and the chemotherapy on the same day.

RISKS:

While you take part in this study, you may be at risk for these side effects. You should discuss them with your doctor.

The drug (s)/procedures used in this study may cause all, some, or none of the side effects listed. There may be other side effects of the drugs/procedures that we do not know of yet.

The side effects may be mild, moderate, or severe. Many side effects go away shortly after the treatment stops, but occasionally, side effects can be serious, long lasting, or may be permanent.

It is not possible to tell which side effect will affect you or how mild or severe the side effect might be. We can only tell you what other people have experienced. Please talk with your doctor about these side effects.

It is very important that you notify your doctor right away about any side effects, problems, or unusual experiences you may have while taking this medication/undergoing this procedure. This will decrease the chance that the side effects continue or become worse. Sometimes there are other medications that we can give you to make the side effects better or make you more comfortable. If severe side effects do develop, you

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and your doctor may decide it is in your best interest to stop taking part in the study.

There may be other risks (other than those outlined below) that are unforeseeable at this time.

Calcitriol:

The only encountered side effects of calcitriol have been an increase in the blood calcium.

Rare (occurs in less than 1% of people, less than 1 person out of 100) side effects of increased levels of calcium include:

- Nausea
- Vomiting
- Sleepiness or even loss of consciousness
- Kidney damage and constipation.
- Additional side effects may include:
- Headache
- Dry mouth
- Muscle and bone pain
- Increased urination
- Increased thirst
- Weight loss
- Increased sensitivity to light
- Runny nose and increases in your blood pressure.
- Formation of kidney stones may also occur.

The risks of simple blood drawing commonly include: the occurrence of discomfort and/or bruising at the site of puncture; and less commonly, the formation of a small blood clot or swelling of the surrounding area, and bleeding from the puncture site. Rarely, fainting and local infection may occur.

Genetic Testing Risks:

Risks of genetic testing include the misuse of personal, genetic information. The study staff have developed processes to better ensure that your genetic information is protected from misuse and that no single person will have access to both your subject number and genetic data. While there can be no absolute guarantees, the risk of misuse of the genetic data is small.

Providing the sample for the genetic test may help in identifying which patients in the future may be more likely to receive benefit from calcitriol treatment.

BENEFITS:

It is unknown if there is any benefit of taking calcitriol along with standard chemotherapy for lung cancer. Your participation in this study may help others in the future because this study may provide answers to how much calcitriol can impact lung cancer therapy

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ALTERNATE COURSES OF ACTION:

Participation in this study is voluntary. You do not have to participate in this study. You may drop out of the study at any time without penalty. By doing so, you will not lose any benefits that you may be entitled to.

If you do not join this study, you have these choices:

1. No treatment, but medications and measures to keep you comfortable. This is called supportive care only.
2. Usual treatment for your disease or condition may be appropriate. This may include treatment with other drugs, drug combinations, surgery, radiation therapy, or possible other new drugs for your type of cancer that may be available in research programs here or at other research centers.

There will be no consequences if you choose not to participate in the study; we will treat you with standard chemotherapy for your cancer. However, if you do participate in the study we encourage you not to withdraw during the study without consulting your physician; doing so may not allow adequate monitoring of your health and you could have side effects from the treatments that may not be detected.

STATEMENT OF RESEARCH RESULTS:

Subject confidentiality will be protected. The data collected at VAMC will be kept in the secure VA computer network with access only to qualified study team members with password access. Any transfer of required data to the central data center at the University of Michigan will be done by removing any identifiers such as name, social security numbers and addresses. All data will be destroyed at the end of 5 years from study completion.

If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent. No information by which you can be identified will be released or published unless required by law. We will let you and your physician know of any important discoveries made during this study which may affect you, your condition, or your willingness to participate in this study.

SPECIAL CIRCUMSTANCES:

There will be not be any costs to you for any additional care that you receive as a participant in this research study. The investigators of this study may have to end your participation in this study for the following reasons; a: if this is not your best interest b. because you are unable to cooperate with the study schema, example: not being able to come in for blood tests because of distance.

The sponsor for this study is the National Cancer Institute.

COMPENSATION:

No compensation is provided for participation in this study.

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RESEARCH SUBJECT'S RIGHTS:

_____ has explained this research study and answered all questions. The risks or discomforts and possible benefits of the study have been described. Other choices of available treatment have been explained. Some veterans are required to pay co-payments for medical care and services provided by VA. These co-payment requirements will continue to apply for VA care and services that are not part of this study.

Participation in this study is entirely voluntary. You may refuse to participate. Refusal to participate will involve no penalty or loss of rights to which individuals are entitled. Participants may withdraw from this study at any time without penalty or loss of VA or other benefits. In the event that you sustain an injury or illness as a result of your participation in this VA approved research study, all necessary medical treatment (except in limited circumstances), will be provided in a VA medical facility. You will be treated for the injury at no cost to you. However, no additional compensation has been set aside. You have not waived any legal rights or released the hospital or its agents from liability for negligence by signing this form.

In case there are medical problems, an injury, or if you have questions, concerns or complaints about the research study, you can contact member(s) of the research study team: Dr. Ramnath can be called at 734-845-5800 during the day and through the UM paging operator at 734-936-4000 (pager 16115) after hours.

You may contact the VA Human Studies coordinator at 734-845-3440 to ask questions about your rights as a research subject and to verify this study is reviewed and approved by the VA. You may also call when research study staff are not available or to discuss your questions or concerns with someone other than study staff. You may learn more about research at the VA Ann Arbor Healthcare System at www.annarbor.research.va.gov

I have been informed about my rights as a research subject, and I voluntarily consent to participate in this study. I will receive a signed copy of this consent form.

X _____
Signature of Subject

X _____
Date

X _____
Signature of Witness
(A witness must observe the subject's signature)

X _____
Witness (Print Name)

X _____
Date

X _____
Signature of person obtaining consent
(Study personnel must be approved by VA IRB.)

X _____
(Print Name)

X _____
Date

IF MORE THAN ONE PAGE IS USED, EACH PAGE (VAF 10-1086) MUST BE CONSECUTIVELY NUMBERED AND SIGNED.

Department of Veterans Affairs HIPAA Authorization Form

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REQUEST FOR PATIENT AUTHORIZATION FOR ACCESS TO PROTECTED HEALTH INFORMATION

- By signing this document, you authorize the Veterans Health Administration (VHA) to provide **Nithya Ramnath** and the research team permission to view and collect your Protected Health Information (medical chart data) for research purposes. This information may include the following:
 Name, Medical record number, dates of test reports, date on study, dates of treatments, off study date, clinic notes; and any other medical records needed by the research team.
****The investigators may view restricted information about you including: HIV infection, Sickle Cell Anemia, drug and/ or alcohol abuse treatment.****
- The research investigators will collect your Protected Health Information for the following specific medical evaluations:
 Initial history and physical exam, X-ray films and reports; pathology reports; laboratory reports; treatment and test results, allergy reports; prescriptions; consultations; clinic notes; and any other medical records needed by the research team.
- Your Protected Health Information, the research data and any identifying linkage will be stored in a secure location.
- You may refuse to sign this authorization and refuse to allow the disclosure of your Protected Health Information. Your refusal will not affect your ability to receive medical care or benefits at the VA Ann Arbor Healthcare System.
- This authorization will expire at the end of the research study.
- This authorization may be revoked at any time by sending a written request to Nithya Ramnath, VAMC, 2215 Fuller Road, Ann Arbor, MI 48105. If you revoke this authorization, Nithya Ramnath, VAMC, 2215 Fuller Road, Ann Arbor, MI 48105 and the research team can continue to use information about you that has been collected. No information will be collected after you revoke the authorization.
- The Ann Arbor VAMC complies with the requirements of the Health Insurance Portability and Accountability Act of 1996 and its privacy regulations and all other applicable laws that protect your privacy. Despite these protections, there is a possibility that your information could be used or disclosed in a way that it will no longer be protected by State and Federal Laws. The research records from this study may be reviewed by the Institutional Review Board and Compliance Monitors of the Ann Arbor VAMC and by other government agencies (including the Government Accounting Office, Office of Human Research Protections and VA Office of Research Oversight).8. Because this study involves material regulated by the FDA (Food and Drug Administration), the FDA may choose to inspect records identifying you as a subject in this research.

X _____
 Signature of Subject

X _____
 (Print Name)

X _____
 Date (mm/dd/yy)