Wake Forest®
School of Medicine

Section of *Hematology and Oncology*

A Pilot Study of Neoadjuvant High Dose Vitamin A for Resectable Non-Small Cell Lung Cancer

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Informed Consent Form to Participate in Research
William J. Petty, M.D., Principal Investigator

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SUMMARY

You are invited to participate in a research study. The purpose of this research is to find out if taking vitamin A increases the number of germinal centers in your tumor and lymph tissues. The specific Vitamin A for this study is retinyl palmitate or retinyl palmitate/vitamin a. Germinal centers are areas where cells that make antibodies mature and may be beneficial to patients with cancer. Germinal centers can be found in the tumors of some patients with lung cancer. Some researchers think that having germinal centers in the tumor could improve the immune system's ability to fight lung cancer. Antibodies are proteins released from the immune system cells that are a key part of the immune systems function. You are invited to be in this study because you have either known or suspected non-small cell lung cancer and it is thought that the cancer should be removed by surgery. Surgery for you type of cancer is standard of care, the research portion of this study is the administration of Vitamin A. Your participation in this research will involve 2 visits and last from about 2 months to about 3-1/2 months depending upon the timing of the surgery.

Participation in this study will involve taking vitamin A for 7 days. Within the next 21 days you will have your surgery. All research studies involve some risks. A risk to this study that you should be aware of is that vitamin A taken in higher doses can cause bleeding gums, sore mouth, bone pain, seizures, dry lips and mouth, diarrhea, double vision and headache. It is unlikely that you will benefit from participation in this study.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. There may be other choices available to you. Some other choices may include surgery without vitamin A addition. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The person in charge of this study is William J. Petty, M.D. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his contact information (phone number) is: [redacted].

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted] or the Research Subject Advocate at Wake Forest at [redacted].

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you have suspected non-small cell lung cancer and it is thought that the cancer should be removed by surgery. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of this research is to find out if taking vitamin A increases the number of germinal centers in your tumor and lymph tissues. Germinal centers are areas where immune cells that make antibodies mature and may be beneficial to patients with cancer.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

180 people at this research site, Wake Forest Baptist Hospital, will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

During your routine care you will be identified in the clinic as a potential participant in the study. If you appear to be eligible you will be screened to make sure you meet all of the study patient criteria and then give this document to review and provide your consent.

You will be randomized into one of the study groups described below. Randomization means that you are put into a group by chance. It is like flipping a coin. You will have an *equal* chance of being placed in any group.

Both Groups

Regardless of the group you are in **you will have your surgery** as a part of your standard care. This means you would have this surgery even if you were not on the study. Once your tumor and lymph node is removed, we will use part of it to evaluate including measurement of lymph node involvement as well as assessment of histopathologic changes. No extra procedures or tissue will be removed in this research study to perform the research.

You will also give blood for research purposes during screening and after completion of Vitamin A.

Vitamin A group

If you are randomized into the vitamin A group, you will take vitamin A for 7 days before your surgery. You must have your surgery within the next 21 days after your last dose of vitamin A. You will be asked to keep track of when you take the vitamin A. After you are finished taking your vitamin A you will give a blood sample, have your vital signs taken and discuss any side effects you have had.

If you take part in this study, you will have the following tests and procedures:

Vitamin A Administration
If you are in the vitamin A group you will take vitamin A for a week (7 days) before your surgery. This would normally not be done and is for research purposes.

Control Group
If you are randomized into the control group you will not take vitamin A.

Blood drawing
You will have approximately 2 tablespoons of blood withdrawn from a vein 2 times. The total amount of blood withdrawn during the study will be approximately 4 tablespoons. These blood draws are for research purposes.

STORAGE OF BIOLOGICAL TISSUE

If you agree to participate in this study, we will draw about 2 tablespoons of blood at two (2) separate times for a total of 4 tablespoons to use for future research. This sample will be kept and may be used in future research to learn more about other diseases. Your sample will be obtained in the Cancer Center, clinic, or pre-operative area at Wake Forest University Baptist Medical Center. The sample will be stored in the laboratory of Dr. Pierre Triozzi and it will be given only to researchers approved by Dr. W. Jeffrey Petty. An Institutional Review Board (IRB) must also approve any future research study using your tissue sample.

Your blood sample will be stored de-identified, which means that no identifying information will be stored with it. Researchers will not know the name, date of birth, medical record number, social security number, etc., of the person who donated the sample.

The research that may be performed with your blood sample is not designed to help you specifically. There is no personal benefit to you from taking part in this aspect of the research study. It might help people who have diseases at some point in the future, but it is not known if this will happen. The results of the research performed with your blood will not be given to you or your doctor. The results will not be put in your medical record. The research using your blood sample will not affect your care.

Your blood sample will be used only for research and will not be sold. The findings from this research may result in the future development of products that are of commercial value. There are no plans to share any of the profits with you which may occur as a result of the research.

I agree to participate in the optional blood draw as described above.
_____ YES
_____ NO
_____ -Participant Initial

In the future, people who do research may need to know more about your health. While the study investigator may give reports about your health, he/she will NOT be given your name, address, phone number, or any other identifying information about who you are, unless you agree to be contacted in the future.

____YES you many contact for future research studies
____NO I do not want to be contacted regarding future research studies.

HOW LONG WILL I BE IN THE STUDY?

You will be in the study for up to about 3 months. You will be followed for approximately 30 days after your last dose of vitamin A to ensure you are not having any unwanted side effect from vitamin A. After that you will be followed for a minimum of 30 days after removal from study or until death, whichever occurs first.

WHAT ARE THE RISKS OF THE STUDY?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. The risks associated with your surgery will be described to you by your physician and/or surgeon. The risks and side effects directly related to this study are taking vitamin A and undergoing blood draws. Side effects from vitamin A at this dose and duration of treatment are uncommon. With longer durations of vitamin A treatment some people have experienced side effects, listed below:

Risk of Vitamin A

Check with your doctor immediately if any of the following side effects occur while taking vitamin A:

- Bleeding from gums or sore mouth
- confusion or unusual excitement
- diarrhea
- dizziness or drowsiness
- double vision
- headache (severe)
- irritability (severe)
- peeling of skin, especially on lips and palms
- vomiting (severe)
- convulsions (seizures)
- fever

Check with your doctor as soon as possible if any of the following side effects occur while taking vitamin A:

- Bone or joint pain
- drying or cracking of skin or lips
- dry mouth
- general feeling of discomfort or illness or weakness
- headache
- increased sensitivity of skin to sunlight
- increase in frequency of urination, especially at night, or in amount of urine
- irritability
- loss of appetite

- loss of hair
- stomach pain
- unusual tiredness
- vomiting

There is no evidence that vitamin A is effective for treating or preventing lung cancer. Some similar medications are used to treat other forms of cancer while other similar medications may actually increase cancer risk.

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

Risks of Blood Draws
You may experience discomfort, bruising and/or bleeding where the needle is inserted. Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions. Frequent donation of blood can result in low iron in your blood (iron deficient anemia).

Risks of Providing Confidential or Private Information
Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

REPRODUCTIVE RISKS AND OTHER ISSUES TO PARTICIPATING IN RESEARCH

Due to known risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, intrauterine device (IUD), DepoProvera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a cervical cap or sponge. We encourage you to discuss this issue further with your physicians if you have any questions.

Pregnant women are excluded from participation in this study. If you are a sexually active woman of childbearing potential and have not been using a reliable method of birth control, a negative pregnancy test is required prior to starting treatment.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

This research is not expected to directly benefit individual subjects, but is likely to yield generalizable knowledge.

WHAT OTHER CHOICES ARE THERE?

This is not a treatment study. Your alternative is to not participate in this study.

The most common procedure for this condition is surgical resection alone and the risks of surgery include pain in the chest, infection, and problems with lung function as well as other risks which should be discussed with your surgeon.

WHAT ARE THE COSTS?

All study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

The purpose of this research study is to obtain data or information on the safety and/or effectiveness of vitamin A; the results will be provided to the sponsor, the Food and Drug Administration and other federal and regulatory agencies as required.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institutes of Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care

provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

WILL YOU BE PAID FOR PARTICIPATING?

You will receive no payment for taking part in this study. However, your parking will be validated for study-related visits.

The findings from this research may result in the future development of products that are of commercial value. There are no plans to provide you with financial compensation or for you to share in any profits if this should occur.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by *Wake Forest Baptist Comprehensive Cancer Center*. The sponsor is providing money or other support to Wake Forest University Health Sciences to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call William J. Petty, M.D. at [redacted].

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and/or information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** results from clinical laboratory tests or exams and demographic information.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study will be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for at least six years after the study is finished. At that time any research information not already in your medical record will either be destroyed or it will be de-identified. Any research information entered into your medical record will be kept for as long as your medical record is kept by the Medical Center. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are

completely finished.

You can tell William J. Petty, M.D. that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

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

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study

at any time. This could be because it is in your best medical interest, your condition worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, William J. Petty, M.D. at [redacted].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted] or the Research Subject Advocate at [redacted]

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm