Department of *Pathology*; Department of *Internal Medicine (Section on Hematology and Oncology)*

A RANDOMIZED, PLACEBO-CONTROLLED PHASE II CLINICAL TRIAL OF OMEGA-3 PUFA DIETARY SUPPLEMENTATION IN PATIENTS WITH STAGE I – III BREAST CARCINOMA

Informed Consent Form to Participate in Research

Edward Levine, MD and Greg Kucera, PhD – Co-principal Investigators

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 breast cancer and are scheduled to undergo surgery to remove your tumor. 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 study is to determine if taking omega-3 polyunsaturated fatty acid (PUFA) supplements affects the levels of omega-3 PUFA in your tumor and in your healthy breast tissue, as well as to determine what effects, good and bad, omega-3 supplements have on your tumor cells.

Omega-3 PUFAs are necessary for the body to work normally; however, they are not produced by the body and must be obtained through the foods that we eat. Omega-3 PUFA supplements derived from fish and fish oil will be used for the purposes of this study.

In this study omega-3 PUFA supplements will be compared to placebo. A placebo is a substance, like a sugar pill, that is not thought to have any effect on your disease or condition. In this study you will either receive the omega-3 PUFA supplements or the placebo, which is not active. Placebos are used in research studies to see if the drug being studied really does have an effect.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

60 people at Wake Forest Baptist Health will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

You will be randomized into one of the study groups described below:

- Omega-3 PUFA supplementation
- Placebo

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. Neither you nor the investigator will know whether you are taking the omega-3 supplement or the placebo. This is done so that a fair evaluation of results can be made. This information is available to the researchers if needed in an emergency.

If you take part in this study, you will be asked to complete the following:

During your routine visit to the clinic prior to undergoing surgery, you will undergo a physical exam and have approximately 4 teaspoons of blood withdrawn through a vein in your arm. You will then be given a supply of capsules (either omega-3 PUFA or placebo). You will be asked to take two capsules per day until your scheduled surgery. You will take the last two capsules the day *before* your surgery is scheduled to occur. You will be given four days' worth of extra capsules so that you will have them in the event your surgery is delayed. If your date of surgery is rescheduled and you do not have enough capsules to last until the day before your rescheduled surgery, the research staff will mail additional capsules to your home.

You should not take any nonsteroidal anti-inflammatory drugs (NSAIDs) such as Advil® (ibuprofen), Motrin® (ibuprofen) and Aleve® (naproxen) or medications containing full dose aspirin while taking the study drug as there is concern that these medications in combination with the omega-3 PUFA supplements can increase your chance of bleeding. If you need to take these medications while you are on this study, please inform the study team.

Every seven days until your surgery, a research nurse will call you to check on the following:

1) if you are experiencing any side effects
2) if you are taking the capsules as directed
3) confirm your surgery date
4) answer any questions you may have

On the day of your scheduled surgery, an additional 4 teaspoons of blood will be drawn. During your surgery, a small sample of your tumor and a small sample of your healthy breast tissue will be obtained for research purposes.

The total amount of blood withdrawn during the study will be approximately 8 teaspoons.

In addition, we would like to study the levels of omega-3 PUFA in tissue samples taken from participants' initial biopsies. If it is determined that you have biopsy tissue available for this

purpose, you can choose whether or not to allow your tissue to be included in this research. If you choose to have your tissue included, your sample will not be labeled with any information that might identify you, and will instead be labeled with a unique identification number instead. If you have tissue available for this research but choose not to allow us to use it, you can still participate in the rest of the study described above, and your decision will not penalize you in any way.

For patients who have additional diagnostic biopsy tissue available for analysis:

I give my permission for tissue from my diagnostic biopsy to be included for analysis in this study:

[ ] Yes [ ] No _____ Initials

In addition, if you are scheduled to have a biopsy at the beginning on the study, you can choose whether or not to allow us to take an additional core biopsy to be included in this research. If you choose to allow us to collect an additional core biopsy to be used for research purposes, your sample will not be labeled with any information that might identify you, and will instead be labeled with a unique identification number. If you choose not to allow us to collect an additional core biopsy sample, you can still participate in the rest of the study described above, and your decision will not penalize you in any way.

For patients who are scheduled to have a biopsy at the beginning of the study:

I give my permission for an additional core biopsy to be collected for research purposes:

[ ] Yes [ ] No _____ Initials

How Long Will I Be in the Study?

The length of participation in this study will vary for each participant depending on their scheduled date of surgery, but will be approximately 2-3 weeks. Each participant will be in the study from the date of enrollment until the day of their surgery. There will be no long-term follow-up.

You can stop participating at any time. 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.

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. Risks and side effects related to taking omega-3 PUFAs include nausea, burping with a fishy aftertaste, and upset stomach. These side effects are generally mild and uncommon.

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.

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.

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 unknown 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.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You are not expected to receive any direct benefit from taking part in this research study. We hope the information learned from this study will benefit other people in the future.

WHAT OTHER CHOICES ARE THERE?

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

What about My Health Information?

In this research study, any new information we collect from you about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes: sex, age, race medical history, current medications, vital signs, height and weight, and blood samples, as well as tumor and healthy tissue samples.

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. Only the following people or organizations will be granted access to your Protected Health Information:

1) The study investigator and his/her staff, or others at Wake Forest University Health Sciences who oversee research

2) Other people or laboratories providing services for this research project on behalf of Wake Forest University Health Sciences and Wake Forest University Baptist Medical Center

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 law.

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. 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 Dr. Edward Levine 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:

[redacted]
Wake Forest School of Medicine
Medical Center Boulevard
Winston-Salem, NC 27157

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.

WHAT ARE THE COSTS?

There are no costs to you for taking part in this study. 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 YOU BE PAID FOR PARTICIPATING?

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

Parking validation will be provided for all study-related visits.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by the American Institute for Cancer Research. 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 (336) 716-3467.

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 [redacted]

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, [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 (336) 716-4542.

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:_____ Date:_____ Time:_____ am pm