NCI Community Oncology Research Program – Kansas City (NCORP-KC)

A RANDOMIZED PHASE III TRIAL COMPARING AXILLARY LYMPH NODE DISSECTION TO RADIATION IN BREAST CANCER PATIENTS (CT1-3 N1) WHO HAVE POSITIVE SENTINEL LYMPH NODE DISEASE AFTER NEOADJUVANT CHEMOTHERAPY

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 that has spread to the lymph nodes under your arm (in the arm pit) and you have been treated with chemotherapy. You may or may not have already undergone surgery to remove the breast cancer and sample the lymph nodes.

Why is this study being done?

Patients with your type of breast cancer usually have neoadjuvant (which means "given before surgery) chemotherapy followed by breast and arm pit surgery to remove any remaining breast cancer. The lymph nodes in the arm pit are examined during surgery and if there is still cancer in the lymph nodes, then the majority of lymph nodes in the arm pit are removed.

The purpose of this study is to examine whether removing some of the lymph nodes from the arm pit, but not removing them all followed with radiation therapy (experimental) will be as good as having the majority of the lymph nodes from the arm pit removed during breast surgery followed with radiation (standard of care).

How many people will take part in the study?

About 2918 participants will take part in this study.

Approval Date 2/8/2018 to 2/7/2019

Assurance#: FWA00003582

What will happen if I take part in this research study?

Before you begin the study
You will need to have the following routine exams, tests or procedures to find out if you can be in 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.

- A medical history (questions about your health, your other medical problems, your medications and any allergies you might have) and a physical examination by your surgeon who is also referred to as your "study doctor." This will include the arm pit on the side of your body where breast cancer is located.
- Mammogram, breast ultrasound

You will then have surgery to examine a few lymph nodes (called sentinel lymph nodes) from your arm pit and at the same time, you may also have your breast cancer surgery (lumpectomy or a mastectomy) to remove any remaining cancer in your breast at the same time. During the surgery your surgeon will remove the sentinel lymph nodes. While you are in the operating room a pathologist (a doctor who examines tissue and body fluids for cancer) may examine the sentinel lymph nodes to see if there is breast cancer remaining there (this is called sentinel lymph node surgery). If no sentinel lymph nodes are found or if they are examined and the cancer is no longer in your sentinel lymph nodes you will not continue with treatment on this study.

If cancer is found in the sentinel lymph nodes, you will be "randomized" into one of the two study groups described below. The randomization may take place during the surgery or it may take place after the surgery is completed. Randomization means that you are put into a group by chance. A computer program will place you in one of the two study groups. Neither you nor your doctor can choose the group you will be in. You will have an equal chance of being placed in either group. If you were randomized during the surgery, you will not know which treatment you were assigned to until after the surgery.

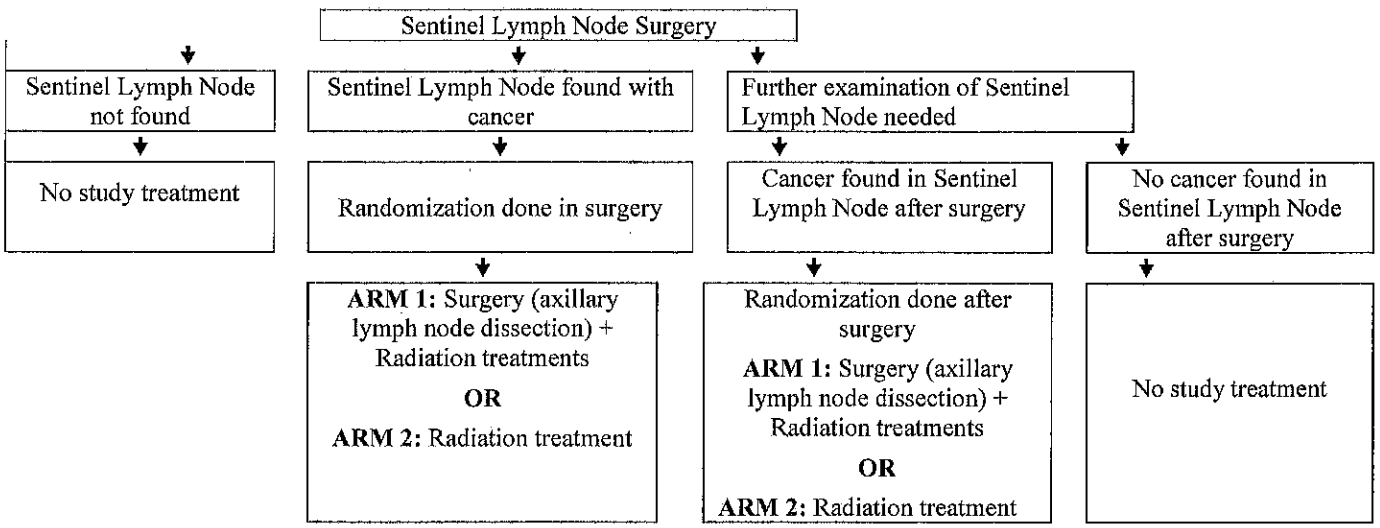
It is possible that the pathologist may need to further examine your sentinel lymph nodes to be sure whether or not there is cancer in them. After your surgery your surgeon will let you know the results. If no cancer is found in any of your sentinel lymph nodes that have been removed and examined, you will not continue with treatment on this study. If there is cancer remaining in your sentinel lymph nodes in your arm pit, you will then be randomized to study treatment as described below.

During the study

If you are randomized to the treatment group called "**Arm 1**" more lymph nodes from your arm pit will be removed (this is called axillary lymph node dissection). If you are randomized to this treatment group after the surgery to examine your lymph nodes, you will have another surgery to remove more lymph nodes from your arm pit (axillary lymph node dissection). You will begin your radiation therapy treatments 3 to 12 weeks after surgery. The radiation treatments will be given 5 days a week over 5 – 6 weeks. The starting day and the details of the treatments will be explained to you by your radiation doctor.

If you are assigned to the treatment group called "**Arm 2**" you will not have any more lymph nodes removed. You will begin your radiation therapy treatments 3 to 12 weeks after surgery. The radiation treatments will be given 5 days a week over 5 – 6 weeks. The starting day and the details of the treatments will be explained to you by your radiation doctor.

The picture below may help you understand this study better.



Test and visits while receiving study treatment

After surgery and during radiation therapy you will have the following tests and procedures done.

- Physical examination that includes the arm pit on the same side of your body where your breast cancer is located. The physical examination will occur about 14 to 42 days after your surgery, before you begin radiation therapy. The examination may be done by your surgeon, radiation doctor, medical oncologist, clinician, Physician Assistant, or Nurse Practitioner.

Tests and visits after study treatment has been completed

- Physical examination that includes the arm pit on the same side of your body where your breast cancer is located. The physical examination will occur every 6 months for the first 2 years, then every year for 3-5 years after your last radiation therapy treatment. The examination may be done by your surgeon, radiation doctor, medical oncologist, clinician, Physician Assistant, or Nurse Practitioner.

How long will I be in the study?

You will be in the study beginning on the day that you receive your treatment assignment, which could be on the day of surgery or several days after. Your radiation therapy will be given over 5 to 6 weeks. After you have completed radiation therapy your surgeon will follow your condition for 3 to 5 years after your last radiation therapy treatment.

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 radiation therapy 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 the surgery or the radiation treatments. 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 that you have while taking part in the study.

Risks and side effects related to the Surgery to remove the lymph nodes in your arm pit (Axillary lymph node dissection) include those which are:

Likely (have been seen in 20% of patients)

- Pain and swelling in the arm or hand on the side of the surgery (lymphedema)

Less Likely (have been seen in 20% or less of patients)

- Problems with wound healing
- Wound infection
- Bruising
- Clear fluid in the wound

Rare, but serious (have been seen in only 2-3% of patients)

- A great amount of bleeding

You will sign a separate consent form before surgery. This will be a standard surgical consent form from the institution where the surgery takes place. The possible risks and side effects of the surgery that you will have will be explained to you in more detail at that time.

Radiation Therapy
Likely (have been seen in 20% of patients)

- Redness and skin irritation similar to a sunburn
- Dryness of peeling skin
- Tenderness in the breast or the chest wall
- Swelling in the breast
- A feeling of tiredness, which is temporary
- Temporary lowering of the number of white blood cells (neutrophils are cells that help your body fight infection)
- Temporary lowering of the number of red blood cells (may cause a feeling of tiredness, and shortness of breath)
- Temporary lowering of the number of blood platelet cells (cells that help your blood clot)

Less Likely (have been seen in 20% or less of patients)

- Soreness or tightness in muscles of the chest wall under the treated breast
- Severe pain at the site of radiation requiring prescription pain relievers

Rare, but serious (have been seen in only 2-3% of patients)

- Leukemia/MDS and secondary malignancies

You will sign a separate consent form before beginning radiation therapy. This will be a standard radiation therapy consent form from the institution where you receive the treatment. The possible risks and side effects of the radiation therapy will be explained to you in more detail at that time.

Reproductive risks: You should not become pregnant while on this study because the radiation therapy in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important you understand that you need to use birth control while on this study. Check with your 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 or suspect you are pregnant wile participating in this study, please inform your treating physician immediately.

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 that not having the lymph nodes removed during breast surgery will be as good as when the lymph nodes are removed during breast surgery, there is no proof of this yet. We do know that the information from this study will help doctors learn more about the treatment of breast cancer that has spread to the lymph nodes. 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

Talk to your doctor about your choices before you decide if you will take part in this study.

Will my medical information be kept private?

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:

- Alliance for Clinical Trials in Oncology (Alliance) and other organizations from the National Clinical Trials Network that take part in this study (including SWOG, ECOG-ACRIN, NCIC-CTG and NRG
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people

If your record is used or shared with the organizations noted above for such purposes, it will be done under conditions that will protect your privacy to the fullest extent possible consistent with laws relating to public disclosure of information and the law-enforcement responsibilities of the agency.

The Alliance has received a Certificate of Confidentiality from the federal government, which will help us to protect your privacy. The Certificate protects against the involuntary release of information about you collected during the course of the study. The researchers involved in this project may not be forced to identify you in any legal proceedings (criminal, civil, administrative, or legislative) at the federal, state, or local level. However, some information may be required by the Federal Food, Drug, and Cosmetic Act, the U.S. Department of Health and Human Services, or for purposes of program review or audit. Also, you may choose to voluntarily disclose the protected information under certain circumstances. For example, if you or your guardian requests the release of information about you in writing (through, for example, a written request to release medical records to an insurance company), the Certificate does not protect against that voluntary disclosure.

What are the costs of taking part in this study?

You and/or your health plan/ insurance company will need to pay for some or all of the costs of treating your cancer in this study. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

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, _____ *[investigator's name(s)],* **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 _____** *[telephone number].*

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.

A Data and Safety Monitoring Board will be regularly meeting to monitor safety and other data related to this study. The Board members may receive confidential patient information, but they will not receive your name or other information that would allow them to identify you by name.

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 or concerns you have about this study. Contact your study doctor _____ *[name(s)]* at _____ *[telephone number].*

For questions about your rights while taking part in this study, call the NCI Community Oncology Research Program – Kansas City Institutional Review Board (a group of people who review the research to protect your rights) at 913-948-5588.

ADDITIONAL STUDIES SECTION

Please note: This section of the informed consent form is about an additional research study that is being done with people who are taking part in the main study. You may choose to take part in this additional study if you want to have not had any surgery to remove your cancer or some of the lymph nodes under the arm pit. You can still be a part of the main study even if you say 'no' to taking part in this additional study. If you have undergone any breast surgery, then you are not able to participate in this additional study.

You can say "yes" or "no" to the following study. Please mark your choice.

Lymphedema Study

The researchers are interested in learning more about one of the common side effects of breast cancer surgery that causes pain and swelling in the arm or hand or breast on the side of the surgery, that is called lymphedema.

a) If you will be having breast conserving surgery (a lumpectomy) you will complete the Breast Lymphedema Symptoms Survey form, which will take about 10 minutes.

b) Everyone on the study will be asked to complete the Lymphedema Signs/Symptoms Form. A research nurse will ask you the questions and record your answers. This will take about 20 minutes to complete.

During your study visits your medical team will also measure your arms and calculate your body mass index (BMI), which is an estimation of body fat based on height and weight.

The questionnaires, arm measurements and BMI calculations will be done after pre-registration before surgery, then every 6 months for 2 years then every year for 5 years after completion of radiation therapy.

1) I agree to complete the lymphedema questionnaires, have my arm measurements taken and have my BMI calculated for the study described above.

_____ Yes _____ No

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at 1-800-4-CANCER (1-800-422-6237).

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.

Release

By signing this form you authorize NCORP-KC to access and obtain information that is required for the study. This may include your medical records, labs, radiologic films and reports and pathology specimens. This authorization to disclose your medical records shall not expire, even upon death, unless specifically revoked in writing by you.

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 10 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.

Participant _____

Participant Signature _____

Date _____

Person Obtaining Consent _____

Person Obtaining Signature_____

Date _____