

Participant Information and Consent Form

For

NSABP B-43

A Phase III Clinical Trial Comparing Trastuzumab Given Concurrently with Radiation Therapy and Radiation Therapy Alone for Women with HER2-Positive Ductal Carcinoma In Situ Resected by Lumpectomy

Sponsor: National Surgical Adjuvant Breast and Bowel Project
(NSABP)

Investigator: Ruby Anne E. Deveras, MD

Sub-Investigators: Boon Y. Chew, MD
Walter J. Durkin, MD
Gregory R. Favis, MD
Abdul Jabbar Sorathia, MD
Richard C. Weiss, MD

**CIRB
APPROVED**

Amend 4 8/5/11

Institution: Halifax Health
Center for Oncology
303 N. Clyde Morris Blvd.
Daytona Beach, Florida 32114
(386) 254-4212 (24 Hour Number)

Study Coordinator: Halifax Health
Center for Oncology
Clinical Trials Department
(386) 254-4213 (Business Hours)

Participant's Initials: _____

This is a clinical trial, a type of research study. You are being asked to take part in this study because you have a very early stage of breast cancer called ductal carcinoma in situ (DCIS). DCIS is also known as intraductal or non-invasive breast cancer. DCIS means that the cancer cells are only in the milk ducts in the breast and have not spread to other breast tissue or to other parts of the body. You are being asked to take part in this study because you have had a lumpectomy to remove the DCIS, and you will be having breast radiation therapy.

Liberty IRB Approved 3/18/10
Liberty IRB Approved 4/15/10, Rev. 1
Liberty IRB Approved 9/09/10, Rev. 2
Liberty IRB Approved 12/23/10, Rev. 3
Liberty IRB Approved 7/28/11, Rev. 4
Liberty IRB Approved 8/25/11, Rev. 5

Participant's Initials _____

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.

Who is conducting the study?

The National Surgical Adjuvant Breast and Bowel Project (NSABP) is conducting this study.

Why is this study being done?

This study is being done to compare the effects, good and/or bad, of adding the drug trastuzumab (also called Herceptin®) to breast radiation therapy. Radiation therapy is the standard treatment for patients with DCIS.

- This study will find out if adding trastuzumab to breast radiation therapy is more effective than radiation therapy without trastuzumab in preventing occurrence of breast cancer in the same breast, in the other breast, or in other parts of the body in patients with HER2-positive DCIS.

The drug trastuzumab is called a targeted therapy because it targets breast cancers that make too much of a protein called HER2. These cancers are called HER2-positive. Too much of the HER2 protein can cause cells to receive extra growth signals. This can turn a normal cell into a cancer cell and can cause cancer cells to grow faster. Trastuzumab has been shown to block the HER2 protein and to slow down or stop the growth of HER2-positive "invasive" breast cancers. ("Invasive" means the cancer has spread outside the milk ducts into other parts of the breast or to other parts of the body.)

Also, there is early information that suggests trastuzumab may be a "radiosensitizer". This means that trastuzumab may help radiation therapy work better in HER2-positive breast cancer. More research is needed to prove this.

In this study, trastuzumab is considered to be investigational (still being researched) because it has not yet been approved by the U.S. Food and Drug Administration (FDA) or Health Canada for use in the treatment of DCIS.

- The only research data on how trastuzumab affects the ovaries in women who have not yet gone through menopause are from studies of trastuzumab given with chemotherapy or after chemotherapy. This study will learn if trastuzumab given without chemotherapy affects the ovaries in women who have not yet gone through menopause.
- If you join the study, we will do special research tests on a sample of your tumor, which has already been removed. The results of these tests should provide NSABP researchers with

Liberty IRB Approved 3/18/10
Liberty IRB Approved 4/15/10, Rev. 1
Liberty IRB Approved 9/09/10, Rev. 2
Liberty IRB Approved 12/23/10, Rev. 3
Liberty IRB Approved 7/28/11, Rev. 4
Liberty IRB Approved 8/25/11, Rev. 5

Participant's Initials _____

information about how genes in the cancer cells may affect the way HER2-positive DCIS responds to treatment.

How many people will take part in the study?

About 2000 women from different cancer centers will take part in this study.

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

Before you begin the study: We must receive results from RUMC that show your DCIS is HER2-positive before you can join the B-43 study. Information about this required HER2 testing is explained in a separate consent form.

You will also need to have the following exams and tests to find out if you can be in the study. These exams and tests 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.

- medical history and physical exam
- mammogram
- consultation with a radiation oncologist (a doctor who specializes in using radiation to treat cancer) to plan your radiation therapy
- if you are a woman of childbearing potential, your doctor or nurse will talk to you about having a pregnancy test

During the study: If all required exams and tests show that you can be in the study, and if you choose to take part, you will be "randomized" into one of the study groups described on the following page. Randomization means that you are put into a group by chance. A computer program will place you in one of 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 are in Group 1, you will receive radiation therapy. Receiving radiation therapy after a lumpectomy is part of regular cancer care for DCIS. There are different ways that radiation therapy can be given. Your radiation therapy treatments will take 3 to 6 weeks to complete depending on the treatment schedule your radiation oncologist decides is best for you. Your doctor will talk with you about your radiation therapy.

If you are in Group 2, you will receive radiation therapy. Receiving radiation therapy after a lumpectomy is part of regular cancer care for DCIS. There are different ways that radiation therapy can be given. Your radiation therapy treatments will take 3 to 6 weeks to complete depending on the treatment schedule your radiation oncologist decides is best for you. Your doctor will talk with you about your radiation therapy.

You will also receive 2 doses of trastuzumab during the time period you receive radiation therapy. You will see a doctor or nurse who will oversee your care related to your trastuzumab. The timing of the trastuzumab doses will depend on your radiation therapy schedule. You will receive Dose 1 within 1 week *before* you start your radiation therapy or *during* the first week of your radiation therapy treatments. The first dose (Dose 1) will be given to you through a vein over 90 minutes. Three weeks after Dose 1 of trastuzumab, and as long as you tolerate Dose 1 with no problems, the second dose of trastuzumab (Dose 2) will be given to you through a vein over 30 minutes.

Summary of study therapy

GROUP 1	GROUP 2
Breast radiation therapy	Breast radiation therapy + Trastuzumab (Dose 1) given through a vein over 90 minutes <i>followed 3 weeks later by</i> Trastuzumab (Dose 2) given through a vein over 30 minutes (if Dose 1 is well tolerated)

For Group 1 and 2 patients:

Hormonal therapy: If your breast cancer is affected by hormones (estrogen or progesterone), your doctor will also prescribe at least 5 years of hormonal therapy for you after surgery. This is part of regular cancer care. The choice of drug to be used for hormonal therapy will be decided by your doctor.

Menstrual history: If you have not gone through menopause, you may be asked to keep track of your menstrual periods during your first 18 months on the study. Your nurse or study doctor will tell you more about this.

As part of the usual care during radiation therapy, you will have physical exams during the weeks you receive radiation therapy. This exam is usually done once a week by the radiation oncology doctor. You may also have tests to check your blood counts. The schedule for these tests and exams may differ depending on the radiation therapy facility where you receive your treatment. Your radiation therapy doctor will tell you more about what to expect during your radiation therapy. Patients in Group 2 will also be seen by the doctor or nurse who will oversee your care related to your trastuzumab.

After completion of study therapy: About 1 month after you complete your radiation therapy, you will have a follow-up exam. You will have a physical exam about every 6 months for 5 years

- Liberty IRB Approved 3/18/10
- Liberty IRB Approved 4/15/10, Rev. 1
- Liberty IRB Approved 9/09/10, Rev. 2
- Liberty IRB Approved 12/23/10, Rev. 3
- Liberty IRB Approved 7/28/11, Rev. 4
- Liberty IRB Approved 8/25/11, Rev. 5

Participant's Initials _____

and then about every 12 months through 10 years from the time you joined the study. You will also have a mammogram once a year for 10 years. (After 10 years, continuing to have a mammogram once a year is an important part of routine health care for any woman.)

How long will I be in the study?

You will be in this study for 10 years. Your study therapy will last about 3-6 weeks depending on your radiation therapy treatment schedule. We would like to keep track of your health until 10 years after you joined the study.

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. It is important to tell the study doctor if you are thinking about stopping so any risks related to the therapy can be evaluated by your doctor. Another reason to tell your doctor is to discuss what follow-up care and testing could be most helpful for you.

You can choose to withdraw in one of two ways. In the first, you can stop your study treatment, but still allow the study doctor to report your health status to the NSABP until 10 years after you joined the study. In the second, you can stop your study treatment and request that no new information be reported to the NSABP.

Also, your study doctor may stop you from taking part in this study if he or she believes it is in the best interest of your health, if you do not follow the study rules, or if the study is stopped by the NSABP.

What side effects or risks can I expect from being in the study?

You may have side effects while on the study. Most of these are listed here, but there may be other side effects that we cannot predict. Side effects will vary from person to person. Everyone taking part in the study will be watched carefully for any side effects.

Side effects may be mild or very serious. Your health care team may give you medicines to help lessen the side effects. Many side effects go away soon after you stop taking the study therapy. In some cases, side effects can be serious, long lasting, or may never go away. *There also is a risk of death.*

The following lists of side effects have been reported by patients receiving trastuzumab. Most of these patients received trastuzumab over a long period of time (6 months or more). Also, most of the patients received trastuzumab at the same time as chemotherapy or after receiving chemotherapy. In the B-43 study, patients who are assigned to receive trastuzumab will receive only 2 doses of trastuzumab over a period of 3 weeks. Therefore, the risk for developing some of these side effects may be lower for B-43 patients. Your study doctor can discuss this with you.

Liberty IRB Approved 3/18/10
Liberty IRB Approved 4/15/10, Rev. 1
Liberty IRB Approved 9/09/10, Rev. 2
Liberty IRB Approved 12/23/10, Rev. 3
Liberty IRB Approved 7/28/11, Rev. 4
Liberty IRB Approved 8/25/11, Rev. 5

Participant's Initials _____

Risks and side effects related to therapy with trastuzumab (Herceptin®):

Less likely

These side effects may occur in **3 to 20%** of patients receiving trastuzumab:

- Lack of enough red blood cells (anemia)
- Fever associated with dangerously low levels of a type of white blood cell (neutrophils)
- The heart stops pumping blood
- A condition in which the heart muscle is abnormally enlarged or thickened
- Decrease in heart's ability to pump blood
- Fluid in the sac around the heart
- Inflammation of the sac around the heart
- Fast heartbeat with regular or irregular rhythm
- Belly pain
- Diarrhea
- Irritation or sores in the lining of the mouth
- Sore throat
- Voice changes
- Nausea
- Vomiting
- Chills
- Fatigue or tiredness
- Difficulty sleeping
- Fever
- Flu-type symptoms (including body aches, fever, chills, tiredness, loss of appetite, cough)
- Chest pain not heart-related
- Pain
- Reaction during the infusion of a drug which may be life-threatening and may result in low blood pressure, fever, chills, difficulty breathing and kidney damage
- Swelling
- Infection
- Increased blood level of a liver or bone enzyme (alkaline phosphatase)
- Increased blood levels of liver enzymes (AST and GGT)
- Increased blood level of a heart muscle protein (troponin I) indicating damage to the heart muscle
- Decrease in the total number of white blood cells (leukocytes), including a decrease in neutrophils or granulocytes, which is a type of white blood cells
- Loss of appetite
- Depression
- Pain in back, joints, bones, or muscles
- Pain in the area of the tumor

Liberty IRB Approved 3/18/10
Liberty IRB Approved 4/15/10, Rev. 1
Liberty IRB Approved 9/09/10, Rev. 2
Liberty IRB Approved 12/23/10, Rev. 3
Liberty IRB Approved 7/28/11, Rev. 4
Liberty IRB Approved 8/25/11, Rev. 5

Participant's Initials _____

- Headache or head pain
- Inflammation or breakdown of the peripheral nerves (those nerves outside of brain and spinal cord) causing numbness, tingling, burning
- Severe damage to the lungs which can lead to fluid in the lungs and can be life-threatening
- Stuffy or runny nose, sneezing
- Sudden constriction of the muscles in the walls of the bronchioles (small airways of the lung)
- Cough
- Shortness of breath
- Decrease in the oxygen supply to a tissue
- Build up of a large amount of fluid between the layers of tissue that line the lungs and chest cavity
- Inflammation of the lungs
- Acne
- Skin rash with the presence of macules (flat discolored area) and papules (raised bump)
- Hives
- High or low blood pressure

Rare but serious

These side effects are **rare but serious**, occurring in **less than 3%** of patients receiving trastuzumab:

- Allergic reaction (an abnormal reaction of the body to substances, called allergens, that are contacted through the skin, inhaled into the lungs, swallowed, or injected)
- Serious type of allergic reaction that may cause breathing difficulty, dizziness, low blood pressure, loss of consciousness, and may be life-threatening
- Abnormal build up of fluid in the lungs
- Scarring of the lungs that can cause shortness of breath and interfere with breathing
- Blood clot in a blood vessel
- Kidney damage

Risks related to radiation therapy: Your radiation therapy doctor will explain the side effects that may result from your radiation therapy. Side effects may also be described in the radiation therapy department's standard consent form that you may also be asked to sign. Although not expected, there is a chance that receiving 2 doses trastuzumab during the time you are receiving radiation therapy may make the side effects related to radiation therapy worse. Your study doctor can tell you more about this.

Risks related to hormonal therapy: As part of regular care for breast cancer, hormonal therapy is given to women whose breast cancer is affected by hormones. Side effects can occur from hormonal therapy. Your study doctor will talk about this with you.

Liberty IRB Approved 3/18/10
Liberty IRB Approved 4/15/10, Rev. 1
Liberty IRB Approved 9/09/10, Rev. 2
Liberty IRB Approved 12/23/10, Rev. 3
Liberty IRB Approved 7/28/11, Rev. 4
Liberty IRB Approved 8/25/11, Rev. 5

Participant's Initials _____

Risks related to fertility and pregnancy: Trastuzumab can affect an unborn baby. Therefore, you should not become pregnant while on this study and for at least 6 months after your last dose of trastuzumab. You should ask about counseling and more information about preventing pregnancy. If you feel you might be pregnant, even though you practiced birth control, you must notify the study doctor immediately. A pregnancy test may be performed. You should not breastfeed a baby while on this study and for at least 6 months after your last dose of trastuzumab.

You should talk to your study doctor about any side effects that you have while taking part in the study.

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 adding trastuzumab to radiation therapy will be more useful in the treatment of HER2-positive DCIS compared to radiation therapy without trastuzumab, there is no proof of this yet. We do know that the information from this study will help doctors learn more about trastuzumab given with radiation therapy as a treatment for HER2-positive DCIS. This information could help future breast 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 this 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.

What about using my tissue for B-43 research?

Tissue required for the HER2 testing is described in a separate consent form. Any tissue remaining after the HER2 testing required for the B-43 study will be sent to the NSABP Division of Pathology. The tissue samples will be stored at the NSABP and will be used for the purposes of the B-43 study. Some of the research tests will be done soon, but others will be done in the future when the best methods are ready to test the samples.

The research that will be done with your tissue sample is not designed to specifically help you. It might help people who have cancer in the future. Reports about research done with your sample will not be given to you or your doctor. These reports will not be put in your health records. The research using your tissue sample will not affect your care. The tissue sample will not be used for genetic research about diseases that are passed on in families.

Your tissue sample will be used only for research and will not be sold. The research done with your sample may help to develop new products in the future, but you will not be paid.

If you decide now that your tissue sample can be kept for this research, you can change your mind at any time. Just *contact your study doctor* and let him or her know that you do not want

Liberty IRB Approved 3/18/10

Liberty IRB Approved 4/15/10, Rev. 1

Liberty IRB Approved 9/09/10, Rev. 2

Liberty IRB Approved 12/23/10, Rev. 3

Liberty IRB Approved 7/28/11, Rev. 4

Liberty IRB Approved 8/25/11, Rev. 5

Participant's Initials _____

the NSABP to use your tissue sample, and it will no longer be used for research. Otherwise, it may be kept until it is used up, or until the NSABP decides to destroy it.

By signing this consent form, you are agreeing to allow any of your tissue remaining after the required HER2 testing for the B-43 study to be sent to the NSABP Division of Pathology for other research related to the B-43 study. *Because the research using this sample is an important part of the B-43 study, it is required for participation in the B-43 study. If you do not agree, you cannot take part in the B-43 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:

- the National Surgical Adjuvant Breast and Bowel Project (NSABP);
- Genentech, Inc. (the company supplying trastuzumab);
- your local Institutional Review Board (IRB), a group of people who review the research study to protect your rights
- the Cancer Trials Support Unit (CTSU), a research group sponsored by the National Cancer Institute (NCI) to provide greater access to clinical trials; and
- government agencies, including the NCI or its authorized representatives, the FDA, the Office for Human Research Protections (OHRP), and Health Canada.. These agencies may review the research to see that it is being done safely and correctly.

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.

Tests, procedures, or drugs for which there is no charge in this study:

Trastuzumab will be provided for this study at no cost to you by Genentech, Inc. through the National Cancer Institute. There will also be no cost to you for the supplies or for the personnel who give you the trastuzumab.

There will be no charge to you or your insurance company for the collection, shipping, testing, and storage of your tissue sample for the research purposes of the B-43 study.

Liberty IRB Approved 3/18/10
Liberty IRB Approved 4/15/10, Rev. 1
Liberty IRB Approved 9/09/10, Rev. 2
Liberty IRB Approved 12/23/10, Rev. 3
Liberty IRB Approved 7/28/11, Rev. 4
Liberty IRB Approved 8/25/11, Rev. 5

Participant's Initials _____

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://www.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 (386)254-4212 (24 hour 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.

The Data Monitoring Committee (DMC), an independent group of experts, will be reviewing the data from this research throughout the study. 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. You may be asked to sign another consent form in response to new information.

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 Dr. Deveras, the Principal Investigator overseeing the study at Halifax Health, your study doctor or the study coordinator about any questions or concerns you have about this study. Contact your study doctor _____ [name(s)] at _____ [telephone number]. You can contact them at:

Liberty IRB Approved 3/18/10
Liberty IRB Approved 4/15/10, Rev. 1
Liberty IRB Approved 9/09/10, Rev. 2
Liberty IRB Approved 12/23/10, Rev. 3
Liberty IRB Approved 7/28/11, Rev. 4
Liberty IRB Approved 8/25/11, Rev. 5

Participant's Initials _____

Halifax Health
Center for Oncology
303 N. Clyde Morris Blvd.
Daytona Beach, FL 32114
(386) 254-4212 (24-Hour Number)

If you have any questions about your rights as a participant in this research study, you can contact

Liberty IRB, Inc.
1450 S. Woodland Blvd. Suite 300A
DeLand, Florida 32720
(386) 740-9278 (Business Hours)

The Liberty Institutional Review Board (IRB) is a committee that has reviewed this research study to help ensure that your rights and welfare as a research participant are protected and that the research study is carried out in an ethical manner.

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

Contact in the future for other research:

Please read the sentence below and think about your choice. After reading the sentence, circle "yes" or "no." If you have questions, please talk to your doctor or health care team member. Remember, no matter what you decide, you may still take part in the B-43 study.

My study doctor (or someone he or she chooses) may contact me in the future to ask me to take part in more research.

YES

NO

Participant's Signature: _____ Date: _____ Time: _____

Where can I get more information?

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.

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

Liberty IRB Approved 3/18/10
Liberty IRB Approved 4/15/10, Rev. 1
Liberty IRB Approved 9/09/10, Rev. 2
Liberty IRB Approved 12/23/10, Rev. 3
Liberty IRB Approved 7/28/11, Rev. 4
Liberty IRB Approved 8/25/11, Rev. 5

Participant's Initials _____

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 receive a copy of this form. If you want more information about this study, ask your study doctor.

Signatures

I have been given a copy of all 12 pages of this form. I have read the consent form or it has been read to me. This information was explained to me and my questions were answered.

I agree to take part in this research study.

Participant's Printed Name

Participant's Signature

Date

Time

Printed Name of Person Conducting Informed Consent Discussion

**Signature of Person
Conducting Informed Consent Discussion**

Date

Time

Physician's Printed Name

Signature of Physician

Date

Time

Liberty IRB Approved 3/18/10
Liberty IRB Approved 4/15/10, Rev. 1
Liberty IRB Approved 9/09/10, Rev. 2
Liberty IRB Approved 12/23/10, Rev. 3
Liberty IRB Approved 7/28/11, Rev. 4
Liberty IRB Approved 8/25/11, Rev. 5

Participant's Initials _____