Comparison of Axillary Lymph Node Dissection With Axillary Radiation for Patients With Node-Positive Breast Cancer Treated With Chemotherapy

This study is currently recruiting participants.

See Contacts and Locations

Verified September 2017 by Alliance for Clinical Trials in Oncology

Sponsor:
Alliance for Clinical Trials in Oncology

ClinicalTrials.gov Identifier:
NCT01901094

First Posted: July 17, 2013
Last Update Posted: October 2, 2017

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

Collaborator:
National Cancer Institute (NCI)

Information provided by (Responsible Party):
Alliance for Clinical Trials in Oncology

• Full Text View
• Tabular View
• No Study Results Posted
• Disclaimer
• How to Read a Study Record

Tracking Information

First Submitted Date  ICMJE  July 12, 2013
First Posted Date  ICMJE  July 17, 2013
Last Update Posted Date  October 2, 2017
Start Date  ICMJE  February 2014
Estimated Primary Completion Date  January 2024  (Final data collection date for primary outcome measure)
Current Primary Outcome Measures  ICMJE
(submitted: November 5, 2014)  Invasive breast cancer recurrence-free interval (IBC-RFI)  [ Time Frame: Up to 5
### Original Primary Outcome Measures
**ICMJE (submitted: July 15, 2013)**

Invasive breast cancer recurrence-free interval (IBC-RFI)  
**Time Frame:** Time from randomization to the first of the following events: invasive ipsilateral, local, regional, or distant recurrence and death due to breast cancer or treatment, assessed up to 5 years after completion of radiation therapy.

### Change History
Complete list of historical versions of study NCT01901094 on ClinicalTrials.gov Archive Site

### Current Secondary Outcome Measures
**ICMJE (submitted: November 4, 2014)**

- Overall survival  
  **Time Frame:** Up to 5 years after completion of radiation therapy.
- Ipsilateral/local/regional invasive breast cancer recurrence (ILR-REC)  
  **Time Frame:** Up to 5 years after completion of radiation therapy.

### Original Secondary Outcome Measures
**ICMJE (submitted: July 15, 2013)**

- Overall survival  
  **Time Frame:** Up to 5 years after completion of radiation therapy.
- Ipsilateral/local/regional invasive breast cancer recurrence (ILR-REC)  
  **Time Frame:** Up to 5 years after completion of radiation therapy.
- Development of arm lymphedema, defined as a 10 % increase in the volume of her ipsilateral arm from its pre-surgery volume using the Breast Lymphedema Symptom Survey  
  **Time Frame:** Up to 2 years post surgery.
- Development of breast lymphedema (in BCT patients) using the Breast Lymphedema Symptom Survey  
  **Time Frame:** Up to 2 years post surgery.
- Radiation dose delivered to supraclavicular and axillary nodes  
  **Time Frame:** Up to 6 weeks post surgery.
- Residual cancer burden (RCB)  
  **Time Frame:** Up to 6 weeks prior to radiation therapy.

### Current Other Outcome Measures
**ICMJE (submitted: November 6, 2014)**

- Development of arm lymphedema if there is a 10% increase in the volume of the ipsilateral arm from its pre-surgery volume  
  **Time Frame:** Up to 5 years after completion of radiation therapy.
- Breast lymphedema (in BCT patients)  
  **Time Frame:** Up to 5 years after completion of radiation therapy.
- Adequacy of radiation fields, dose delivered to supraclavicular and axillary nodes  
  **Time Frame:** Up to 5 years after completion of radiation therapy.
- Residual cancer burden (RCB)  
  **Time Frame:** Up to 5 years after completion of radiation therapy.

### Original Other Outcome Measures
**ICMJE**

Not Provided

### Descriptive Information

#### Brief Title
Comparison of Axillary Lymph Node Dissection With Axillary Radiation for Patients With Node-Positive Breast Cancer Treated With Chemotherapy

#### Official Title
A Randomized Phase III Trial Comparing Axillary Lymph Node Dissection to Axillary Radiation in Breast Cancer Patients (cT1-3 N1) Who Have Positive Sentinel Lymph Node Disease After Neoadjuvant Chemotherapy

#### Brief Summary
This randomized phase III trial studies axillary lymph node dissection to see how breast cancer treated with neoadjuvant chemotherapy followed by surgery. Lymph nodes in breast cancer patients. Radiation therapy uses high-energy x-rays to kill tumor cells.

#### Detailed Description
Study Outline:
All patients will undergo surgery to identify sentinel lymph node(s). If a lymph node has cancer, the patient will be registered/randomized intra-operatively.

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Patients who do not have a sentinel lymph node identified will not be registered/randomized to the study.

Patients whose sentinel lymph node status is cannot be/is not determined intra-operatively, and have not undergone ALND, but had at least one lymph node (sentinel or non-sentinel) found to be positive on final pathology review will be registered/randomized post-operatively.

Patients whose sentinel lymph node status is found to be negative intra-operatively and have not undergone ALND, but had at least one lymph node (sentinel or non-sentinel) found to be positive on final pathology review will be registered/randomized post-operatively.

ALND is not to be performed prior to registration/randomization.

Patients who are determined to have negative lymph nodes on final pathology will not be registered/randomized, but can be offered participation in another cooperative group trial.

The primary and secondary objectives of the study are described below. Please see the “Arms” section for a detailed description of the treatment regimens.

Primary Objective:
To evaluate whether radiation to the undissected axilla and regional lymph nodes but not to the dissected axilla in terms of invasive breast cancer recurrence-free interval in patients with positive SLN(s) after completion of neoadjuvant chemotherapy

Secondary Objectives:
To evaluate whether radiation to the undissected axilla and regional lymph nodes but not to the dissected axilla in terms of the incidence of invasive loco-regional recurrences in patients with a positive SLN(s) after completion of neoadjuvant chemotherapy

To obtain an estimate of the distribution of residual disease burden scores for each treatment arm

To estimate the distribution of overall survival for each treatment arm

Patients may receive adjuvant and ancillary therapy as appropriate per the protocol.

Adjuvant Therapy:

Adjuvant endocrine therapy: Patients with hormone receptor (ER and/or PR) positive disease should receive a minimum of 5 years of standard endocrine therapy (experimental agents/regimens are not permitted). Endocrine therapy should begin following completion of neoadjuvant chemotherapy and surgery, either before, during or after radiation therapy at the discretion of the oncologist. Selection of the agents is at the treating physician’s discretion.

Patients with HER2 positive disease should complete a total of one year of trastuzumab therapy (over the neoadjuvant and adjuvant period).

Chemotherapy, biologic therapy or vaccine therapy in the adjuvant setting is not allowed. Patients who wish to receive any of these therapies after surgery must go off study at the time of their initiation.

Ancillary Therapy:

Patients should receive full supportive care, including transfusions of blood and blood products, erythropoetin (unless otherwise specified in the protocol), antibiotics, antiemetics, etc. when appropriate.

Patients are followed up for 5 years after completion of radiation therapy.

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| Study Design| Allocation: Randomized  
              Intervention Model: Parallel Assignment  
              Masking: None (Open Label)  
              Primary Purpose: Treatment |
### Condition
- Stage II Breast Cancer
- Stage IIIA Breast Cancer

### Intervention
- Procedure: Axillary Lymph Node Dissection (ALND)
- Radiation: Nodal Radiation Therapy
- Radiation: Axillary Radiation Therapy

### Study Arms
- **Arm 1:** ALND + nodal radiation therapy
  - **Surgery:** For patients randomized to axillary lymph node dissection (ALND), it is recommended that a complete level I and II dissection with resection of a minimum of a total of 8 lymph nodes (SLN and ALND together) be done. Level III dissection is not required, but may be performed at the discretion of the surgeon. If fewer than 8 lymph nodes (SLN and ALND together) are resected, then the patient will discontinue protocol treatment.
  - **Radiation Therapy:** Radiation is delivered to the breast/chest wall, undissected axilla, supraclavicular nodes and internal mammary nodes in the first 3 intercostal spaces. Treatment will be given 5 days a week over 5-6 weeks.
  - **Interventions:**
    - Procedure: Axillary Lymph Node Dissection (ALND)
    - Radiation: Nodal Radiation Therapy
- **Arm 2:** Axillary radiation and nodal radiation therapy
  - **Radiation Therapy:** Radiation is delivered to the breast/chest wall, full axilla including Levels I, II, III, supraclavicular nodes and internal mammary nodes in the first 3 intercostal spaces. Treatment will be given 5 days a week over 5-6 weeks.
  - **Interventions:**
    - Radiation: Nodal Radiation Therapy
    - Radiation: Axillary Radiation Therapy

### Publications *

* Includes publications given by the data provider as well as publications identified by ClinicalTrials.gov Identifier (NCT Number) in Medline.

### Recruitment Information
- **Recruitment Status:** Recruiting
- **Estimated Enrollment:** 2918
- **Completion Date:** Not Provided
- **Estimated Primary Completion Date:** January 2024 (Final data collection date for primary outcome measure)
Eligibility Criteria

Pre-Registration Eligibility Criteria:

1. Patients ≥ 18 years of age
2. Clinical stage T1-3 N1 M0 breast cancer at diagnosis (prior to the start of neoadjuvant chemotherapy) by American Joint Committee on Cancer (AJCC) staging 7th edition
3. No inflammatory breast cancer
4. No other malignancy within 5 years of registration with the exception of basal cell or squamous cell carcinoma in situ of the cervix
5. All patients must have had an axillary ultrasound with fine needle aspiration (FNA) or core needle biopsy of axillary lymph nodes documenting axillary metastasis at the time of diagnosis, prior to or at most 14 days after starting neoadjuvant chemotherapy. Note: Biopsy of intramammary nodes does not fulfill eligibility criteria.
6. Patients must have had estrogen receptor, progesterone receptor and human epidermal growth factor receptor 2 (HER2) status by immunohistochemistry [IHC] and/or fluorescence in situ hybridization [FISH] evaluated on diagnostic core biopsy prior to start of neoadjuvant chemotherapy. Note: If HER2 status has not been clearly determined (ie equivocal/indeterminate), then patients should not be enrolled.
7. Patients must have completed all planned chemotherapy prior to surgery. Sandwich chemotherapy is not allowed (i.e. chemotherapy planned to be given after surgery). Patients must have completed at least 4 cycles of neoadjuvant chemotherapy consisting of an anthracycline and/or taxane-based regimen without evidence of disease progression in the breast or the lymph nodes. NOTE: Delays/dose modifications due to toxicities/adverse events are allowed as long as a minimum of 4 cycles of neoadjuvant chemotherapy is administered. More than 4 cycles of NAC may be administered at the discretion of the treating medical oncologist.
8. Patients with HER-2 positive tumors must have received neoadjuvant trastuzumab or trastuzumab + pertuzumab or other approved anti-HER2 therapy (either with all or with a portion of the neoadjuvant chemotherapy regimen). Therapy must be Food and Drug Administration (FDA)-approved targeted anti-HER2 therapy, but additional therapies are allowed as are non-trastuzumab regimens if administered in the context of an Institutional Review Board (IRB)-approved clinical trial.
9. All patients must have a clinically negative axilla (no palpable lymph nodes or bulky adenopathy) on physical examination documented at the completion of neoadjuvant chemotherapy. NOTE: An ultrasound of the axilla is not required at completion of neoadjuvant chemotherapy. If performed, its findings do NOT impact eligibility.
10. No neoadjuvant endocrine therapy
11. No neoadjuvant radiation therapy
12. No sentinel lymph node (SLN) surgery/excisional biopsy for pathological confirmation of axillary status prior to or during neoadjuvant chemotherapy
13. No prior history of ipsilateral breast cancer (invasive disease or ductal carcinoma in situ [DCIS]). Lobular carcinoma in situ (LCIS) and benign breast disease is allowed.
14. No prior ipsilateral axillary surgery, such as excisional biopsy of lymph node(s) or treatment of hidradenitis.
15. No history of prior or concurrent contralateral invasive breast cancer.
16. Patients must not be pregnant or nursing. A negative pregnancy test is required prior to registration for women of childbearing potential. Note: Perimenopausal women must be amenorrheic for > 12 months to be considered not of childbearing potential.
17. Eastern Cooperative Oncology Group (ECOG) (Zubrod) performance status 0-1.
18. Required Pre-Registration Laboratory Values:
   - Serum or urine beta-human chorionic gonadotropin (ß-HCG)
   - Negative in women of child-bearing potential

Intra-Operative Registration/Randomization Criteria:
1. Breast surgery (lumpectomy or mastectomy) and sentinel lymph node surgery must be completed within 56 days of the completion of neoadjuvant chemotherapy.

2. A minimum of 1 sentinel node and a maximum of 6 total nodes (sentinel + non-sentinel) are identified and excised by the surgeon. Patients who do not have an identifiable sentinel lymph node will not proceed to Registration/Randomization.

3. At least one lymph node (sentinel or non-sentinel) with a metastasis greater than 0.2 mm in greatest dimension identified on intra-operative pathologic assessment. Note: Isolated tumor cells (metastases less than or equal to 0.2 mm) will be treated as node negative disease (N0i+). Axillary lymph node dissection [ALND] is not to be performed prior to Registration/Randomization.

Post-Operative Registration/Randomization Criteria:
1. For cases where ALND has not been performed and one of the following is true:
   - intra-operative evaluation of sentinel lymph node could not be/was not performed and final pathology identified a positive lymph node (sentinel or non-sentinel) with metastasis greater than 0.2 mm on hematoxylin and eosin stain (H & E) OR
   - lymph node (sentinel or non-sentinel) considered negative on intra-operative evaluation was found to be positive on final pathology (with metastasis greater than 0.2 mm on H & E)

Breast surgery (lumpectomy or mastectomy) and sentinel lymph node surgery must be completed within 56 days of the completion of neoadjuvant chemotherapy.

At least one lymph node (sentinel or non-sentinel) with a metastasis greater than 0.2 mm in greatest dimension identified by H&E staining on final pathology (for cases where intra-operative evaluation was not performed, or was negative and completion dissection was not performed).

Among the minimum of 1 and the maximum of 6 nodes (sentinel or non-sentinel) identified and excised by the surgeon, no more than 8 lymph nodes (sentinel and non-sentinel) were found by the pathologists to have been actually excised. Note: Isolated tumor cells (metastases less than or equal to 0.2 mm) will be treated as node negative disease (N0i+).

For those patients who also undergo contralateral breast surgery, if invasive disease is found, the patient is not eligible for registration/randomization.

### Sex/Gender
- **Sexes Eligible for Study:** All

### Ages
- **18 Years and older (Adult, Senior)**

### Accepts Healthy Volunteers
- **No**

### Contacts
- **Contact:** Judy Boughey, MD  507-284-3629

### Listed Location Countries
- **Canada, Puerto Rico, United States**

### Administrative Information

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**Other Study ID Numbers**
- **A011202**
- **U10CA031946 (U.S. NIH Grant/Contract)**
- **NCI-2013-00875 (Registry Identifier: Clinical Trial Reporting Program)**

**Has Data Monitoring Committee**
- **Yes**
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Data element required by the **International Committee of Medical Journal Editors** and the World Health Organization ICTRP