CTSU Cancer Trials Support Unit
A SERVICE OF THE NATIONAL CANCER INSTITUTE
Linking practice to progress

NSABP B-51/RTOG 1304

Breast Cancer
Protocol Date: 02/24/16 (Amendment #3)

A Randomized Phase III Clinical Trial Evaluating Post-Mastectomy Chestwall and Regional Nodal XRT and Post-Lumpectomy Regional Nodal XRT in Patients with Positive Axillary Nodes Before Neoadjuvant Chemotherapy Who Convert to Pathologically Negative Axillary Nodes After Neoadjuvant Chemotherapy

Eligibility

- Patients with pathologic confirmation of axillary nodal involvement at presentation (before neoadjuvant therapy) based on a positive FNA (demonstrating malignant cells) or positive core needle biopsy (demonstrating invasive adenocarcinoma). Patients may not have had documentation of axillary nodal positivity by sentinel node biopsy (before neoadjuvant therapy).
- Patient must have clinically T1-3, N1 breast cancer at the time of diagnosis (before neoadjuvant therapy).
- Patients must provide consent, be female, be ≥ 18, and have an ECOG PS of 0 or 1.
- Patients must have had ER analysis performed on the primary breast tumor before neoadjuvant therapy according to current ASCO/CAP Guideline Recommendations for hormone receptor testing. If negative for ER, assessment of PgR must also be performed according to current ASCO/CAP Guideline Recommendations for hormone receptor testing.
- Patients who have a primary tumor that is either HER2-positive or HER2-negative are eligible. HER2 testing must have been completed prior to neoadjuvant chemotherapy.
- Patient must have completed a minimum of 8 weeks of standard neoadjuvant chemotherapy consisting of an anthracycline and/or taxane-based regimen.
- For patients who receive adjuvant chemotherapy after surgery, a maximum of 12 weeks of intended chemotherapy may be administered but must be completed before randomization. If treatment is delayed, chemotherapy must be completed within 14 weeks.
- Patients with HER2-positive tumors must have received neoadjuvant anti-HER2 therapy (either with all or with a portion of the neoadjuvant chemotherapy regimen), unless medically contraindicated.
- At the time of definitive surgery, all removed axillary nodes must be histologically free from cancer. For a list of acceptable procedures see Section 5.2.12.
- Patients with pathologic staging of ypN0(i+) or ypN0(mol+) are eligible.
- Patients who have undergone either a total mastectomy (including nipple sparing mastectomy) or a lumpectomy are eligible.
- For patients who undergo lumpectomy, the margins of the resected specimen or re-excision must be histologically free of invasive tumor and DCIS as determined by the local pathologist. Additional operative procedures may be performed to obtain clear margins. If tumor is still present at the resected margin after re-excision(s), the patient must undergo total mastectomy to be eligible. (Patients with margins positive for LCIS are eligible without additional resection.)
- For patients who undergo mastectomy, the margins must be histologically free of residual (microscopic or gross) tumor.
- The interval between the last surgery for breast cancer (including re-excision of margins) and randomization must be no more than 56 days. Also, if adjuvant chemotherapy was administered, the interval between the last chemotherapy treatment and randomization must be no more than 70 days.
- The patient must have recovered from surgery with the incision completely healed and no signs of infection.
- If adjuvant chemotherapy was administered, chemotherapy-related toxicity that may interfere with delivery of radiation therapy should have resolved.
- Patients must not have definitive clinical or radiologic evidence of metastatic disease.
- No T4 tumors including inflammatory breast cancer.
- No documentation of axillary nodal positivity before neoadjuvant therapy by sentinel node biopsy alone.
- Patients must not have N2 or N3 disease detected clinically or by imaging.
- Patients must not have histologically positive axillary nodes post neoadjuvant therapy.
- Patients must not have microscopic positive margins after definitive surgery.
- Patients must not have a synchronous or previous contralateral invasive breast cancer or DCIS. (Patients with synchronous and/or previous contralateral LCIS are eligible.)
- No prior history, not including the index cancer, of ipsilateral invasive breast cancer or ipsilateral DCIS treated with radiation therapy. (Patients with synchronous or previous ipsilateral LCIS are eligible.)
- No prior history of non-breast malignancies (except for in situ cancers treated only by local excision and basal cell and squamous cell carcinomas of the skin) within 5 years prior to randomization.
- Patient may not be receiving any radiation therapy for the currently diagnosed breast cancer prior to randomization.
- No continued use of sex hormonal therapy, e.g., birth control pills, ovarian hormone replacement therapy. Patients are eligible if these medications are discontinued prior to randomization (see Section 5.1).
- Patients must not have had prior breast or thoracic RT for any condition.
- No active collagen vascular disease, specifically dermatomyositis with a CPK level above normal or with an active skin rash, systemic lupus erythematosis, or scleroderma.
- Patients may not be pregnant or lactating at the time of study entry**.**
- No other non-malignant systemic disease that would preclude the patient from receiving study treatment or would prevent required follow-up.
- Patients must not have psychiatric or addictive disorders or other conditions that, in the opinion of the investigator, would preclude the patient from meeting the study requirements.

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Required Pre-Study Laboratory / Tests

(Tests, exams, and other requirements prior to randomization)

• CBC/diff/Platelets*	within 4 weeks prior to randomization
• Determination of hormone receptor status (Section 5.2.7)	(prior to giving neoadjuvant therapy)
• HER2 analysis (Section 5.2.8)	(prior to giving neoadjuvant therapy)
• History and physical exam	within 4 weeks prior to randomization
• Assessment of performance status	within 4 weeks prior to randomization
• Menopausal status (at the time of breast cancer diagnosis)	within 4 weeks prior to randomization
• Pregnancy status	within 2 weeks prior to randomization
• Imaging	CT chest/abdomen/pelvis **and** bone scan or PET/CT scan; between diagnosis and randomization
• Bilateral breast imaging	mammogram or MRI; within 12 months
• Tumor blocks (from primary breast tumor and from definitive surgery [if residual disease > 0.5 cm])	Must be requested before study entry and submitted within 90 days following randomization (Section 7.1)

* For patients receiving adjuvant chemotherapy, testing must be done at least 3 weeks from last dose of chemotherapy

THIS INFORMATION IS INTENDED TO BE USED AS A SCREENING TOOL *ONLY* AND SHOULD NOT BE USED IN PLACE OF THE PROTOCOL.

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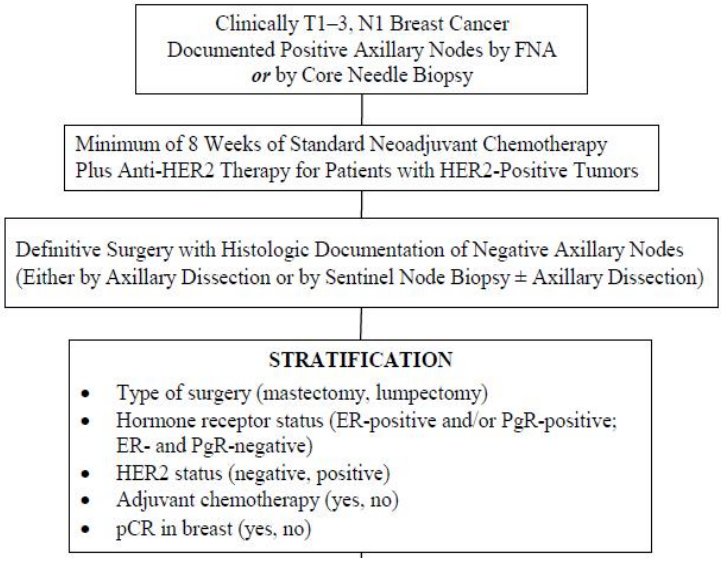
Schema



Patients will be randomized to one of the following:

Arm 1 (with no regional nodal irradiation):

Group 1A (post-lumpectomy):
- Radiation therapy-Whole breast XRT + boost
- Systemic therapy as appropriate (e.g., hormonal therapy, anti-HER2 therapy)

Group 1B (post-mastectomy):
- Systemic therapy as appropriate (e.g., hormonal therapy, anti-HER2 therapy)

Arm 2 (with regional nodal irradiation):

Group 2A (post-lumpectomy):
- Radiation therapy-Whole breast XRT + boost + regional nodal XRT
- Systemic therapy as appropriate (e.g., hormonal therapy, anti-HER2 therapy)

Group 2B (post-mastectomy):
- Radiation therapy-Chest wall XRT + regional nodal XRT
- Systemic therapy as appropriate (e.g., hormonal therapy, anti-HER2 therapy)