

## Fast Facts

### **NSABP B51: 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**

#### **Inclusion Criteria**

##### **Patient selection guidelines**

- Patients should have a life expectancy of at least 10 years, excluding their diagnosis of breast cancer. (Comorbid conditions should be taken into consideration, but not the diagnosis of breast cancer.)
- Women of reproductive potential must agree to use an effective non-hormonal method of contraception during radiation therapy.
- *Submission of tumor samples is required for all patients* (see Section 7.1). Therefore, the local pathology department policy regarding release of tumor samples must be considered in the screening process.

##### **Conditions for patient eligibility**

1. The patient must have signed and dated an IRB-approved consent form.
2. The patient must be female.
3. The patient must be  $\geq 18$  years old.
4. The patient must have an ECOG performance status of 0 or 1 (see Appendix A).
5. Patient must have clinically T1-3, N1 breast cancer at the time of diagnosis (before neoadjuvant therapy). Clinical axillary nodal involvement can be assessed by palpation, ultrasound, CT scan, MRI, PET scan, or PET/CT scan.
6. Patient must have had pathologic confirmation of *axillary nodal involvement* at presentation (before neoadjuvant therapy) based on either a positive FNA (demonstrating malignant cells) or positive core needle biopsy (demonstrating invasive adenocarcinoma). The FNA or core needle biopsy can be performed either by palpation or by image guidance. *Documentation of axillary nodal positivity by sentinel node biopsy (before neoadjuvant therapy) is not permitted.*
7. 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 (<http://www.asco.org>).
8. Patients must have had HER2 testing performed on the primary breast tumor before neoadjuvant chemotherapy according to the current ASCO/CAP Guideline Recommendations for Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer (<http://www.asco.org>). Patients who have a primary tumor that is either HER2-positive or HER2-negative are eligible.
9. Patient must have completed a minimum of 8 weeks of standard *neoadjuvant* chemotherapy consisting of an anthracycline and/or taxane-based regimen.
10. 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 delays occur, chemotherapy must be completed within 14 weeks.) The dose and schedule of the adjuvant chemotherapy are at the investigator's discretion. *Note: It is preferred that all intended chemotherapy be administered in the neoadjuvant setting.*
11. 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.

12. At the time of definitive surgery, all removed axillary nodes must be histologically free from cancer. Acceptable procedures for assessment of axillary nodal status at the time of surgery include:
- axillary node dissection;
  - sentinel node biopsy alone provided that at least 2 sentinel lymph nodes are removed. Removal of at least 3 sentinel lymph nodes and use of dual tracer for lymphatic mapping are strongly recommended; or
  - sentinel node biopsy followed by axillary node dissection.

Note: Patients are eligible whether there is residual invasive carcinoma in the surgical breast specimen or whether there is evidence of pathologic complete response.

*Patients who are found to be pathologically node-positive at the time of surgery, based on sentinel node biopsy alone, are candidates for A011202, a study developed by the Alliance in Oncology, an NCI Cooperative Group. If A011202 is open at the investigator's institution, patients should be approached about participating in the A011202 study.*

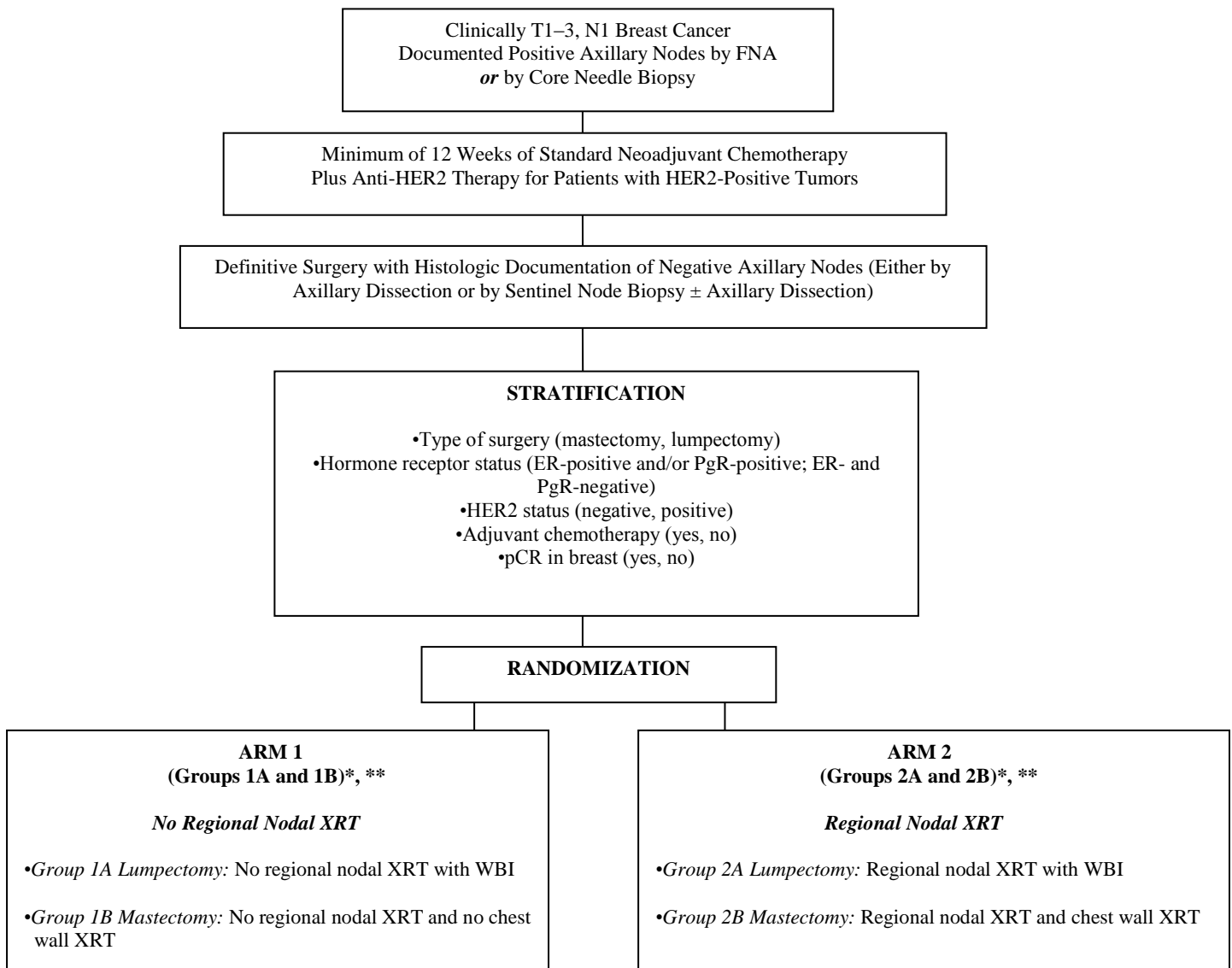
13. Patients with pathologic staging of ypN0(i+) or ypN0(mol+) are eligible.
14. Patients who have undergone either a total mastectomy or a lumpectomy are eligible. (Patients who have had a nipple-sparing mastectomy are eligible.)
15. For patients who undergo lumpectomy, the margins of the resected specimen 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.)
16. For patients who undergo mastectomy, the margins must be histologically free of residual (microscopic or gross) tumor.
17. The interval between the last surgery for breast cancer (including re-excision of margins) and randomization must be no more than 70 days. Also, *if adjuvant chemotherapy was administered*, the interval between the last chemotherapy treatment and randomization must be no more than 70 days.
18. The patient must have recovered from surgery with the incision completely healed and no signs of infection.
19. If adjuvant chemotherapy was administered, chemotherapy-related toxicity that may interfere with delivery of radiation therapy should have resolved.

### **Conditions for patient ineligibility**

1. Definitive clinical or radiologic evidence of metastatic disease.
2. T4 tumors including inflammatory breast cancer.
3. Documentation of axillary nodal positivity before neoadjuvant therapy by sentinel node biopsy alone
4. N2 or N3 disease detected clinically or by imaging.
5. Patients with histologically positive axillary nodes post neoadjuvant therapy.
6. Patients with microscopic positive margins after definitive surgery.
7. Synchronous or previous contralateral invasive breast cancer or DCIS. (Patients with synchronous and/or previous contralateral LCIS are eligible.)
8. Any 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.)
9. 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.
10. Any radiation therapy for the currently diagnosed breast cancer prior to randomization.

11. Any 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).
12. Prior breast or thoracic RT for any condition.
13. Active collagen vascular disease, specifically dermatomyositis with a CPK level above normal or with an active skin rash, systemic lupus erythematosus, or scleroderma.
14. Pregnancy or lactation at the time of study entry. (*Note: Pregnancy testing must be performed within 2 weeks prior to randomization according to institutional standards for women of childbearing potential.*)
15. Other non-malignant systemic disease that would preclude the patient from receiving study treatment or would prevent required follow-up.
16. Psychiatric or addictive disorders or other conditions that, in the opinion of the investigator, would preclude the patient from meeting the study requirements.

**SCHEMA**



**\* Patients will be randomized to one of the following:**

- **Arm 1**
  - Radiation therapy for Group 1A  
Whole breast irradiation + boost
  - No radiation therapy for Group 1B
  
- **Arm 2**
  - Radiation therapy for Group 2A  
Whole breast irradiation + boost and regional nodal irradiation
  - Radiation therapy for Group 2B  
Chest wall and regional nodal irradiation

\*\* All patients will receive additional systemic therapy as planned (i.e., hormonal therapy for patients with hormone receptor-positive breast cancer and trastuzumab or other anti-HER2 therapy for patients with breast cancer that is HER2-positive).

**Pre-Study Parameters**

1. History and physical including, ECOG PS, height, weight and menopausal status.
2. Hormone receptor and HER2 status prior to neo-adjuvant therapy.
3. CBC and differential, pregnancy test
4. Bilateral breast imaging.
5. CT of chest/abdomen/pelvis AND bone scan or PET/CT.
6. Mandatory submission of tumor materials (*prior to study entry*, blocks must be requested and local pathology department must agree to release per Section 7.1)