Cancer Research Consortium of West Michigan
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FAST FACTS

A011202: 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

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 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 of the skin treated with local resection only or carcinoma in situ of the cervix.
5. All patients must have had an axillary ultrasound with 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 HER2 status (by IHC and/or ISH) evaluated on diagnostic core biopsy prior to start of neoadjuvant chemotherapy.
   Note: If HER2 status has not been clearly determined (i.e. equivocal/indeterminate), then patients should not be enrolled.
7. Patients must have completed all planned neoadjuvant chemotherapy prior to surgery. Planned sandwich chemotherapy is not allowed (i.e. anthracycline/Cytoxan or taxane 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-HER-2 therapy (either with all or with a portion of the neoadjuvant chemotherapy regimen). Therapy must be FDA-approved targeted anti-HER2 therapy, but additional therapies are allowed as are non-trastuzumab regimens if administered in the context of an IRB-approved clinical trial. Completion of a course of trastuzumab, pertuzumab, TD-M1 and/or other anti-Her2 neu therapy after surgery is allowed.
9. All patients must have a clinically negative axilla (no 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 more than 8 weeks of neoadjuvant endocrine therapy prior to the start of neoadjuvant chemotherapy.
11. No neoadjuvant radiation therapy.
12. No 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 DCIS). 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. Benign breast disease, LCIS or DCIS of contralateral breast is allowed. Ipsilateral multifocal or multicentric disease is allowed.
16. Patients must not be pregnant or nursing.
    Note: Peri-menopausal women must be amenorrheic for > 12 months to be considered not of childbearing potential.
17. ECOG (Zubrod) Performance Status 0-1.

Intra-operative registration/randomization criteria

1. Breast surgery (lumpectomy or mastectomy) and sentinel lymph node surgery must be completed within 112 days of the completion of the last dose of neoadjuvant chemotherapy. No additional chemotherapy and no radiation therapy are allowed in the intervening 112 days. Endocrine therapy or HER2-targeted therapy as a bridge between cytotoxic and surgical treatments are allowed. No experimental agents are allowed during this time.
2. A minimum of 1 sentinel node and a maximum of 8 total nodes (sentinel + non-sentinel) are identified and excised during the sentinel lymph node surgery. More than 8 nodes identified by either surgeon or pathologist is not allowed.
   Note: 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) excised during sentinel lymph node surgery 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+).
   Note: If on final pathology, more than 8 lymph nodes are seen pathologically, then the patient should discontinue study (see Section 14.0)
   ALND is not to be performed prior to Registration/Randomization.
   Note: Patients for whom no positive lymph nodes (sentinel or non-sentinel) are found during sentinel lymph node surgery will not proceed to registration/randomization and can be considered for discussion of the NRG NSABP B-51/RTOG 1304 study "A Randomized Phase III Clinical Trial Evaluating the Role of Post-mastectomy Chest Wall and Regional Nodal XRT and Post-lumpectomy Regional Nodal XRT in Patients with Documented Positive Axillary Nodes Before Neoadjuvant Chemotherapy Who Convert to Pathologically Negative Axillary Nodes After Neoadjuvant Chemotherapy" (See Section 14.0).

Post-operative registration/randomization criteria:

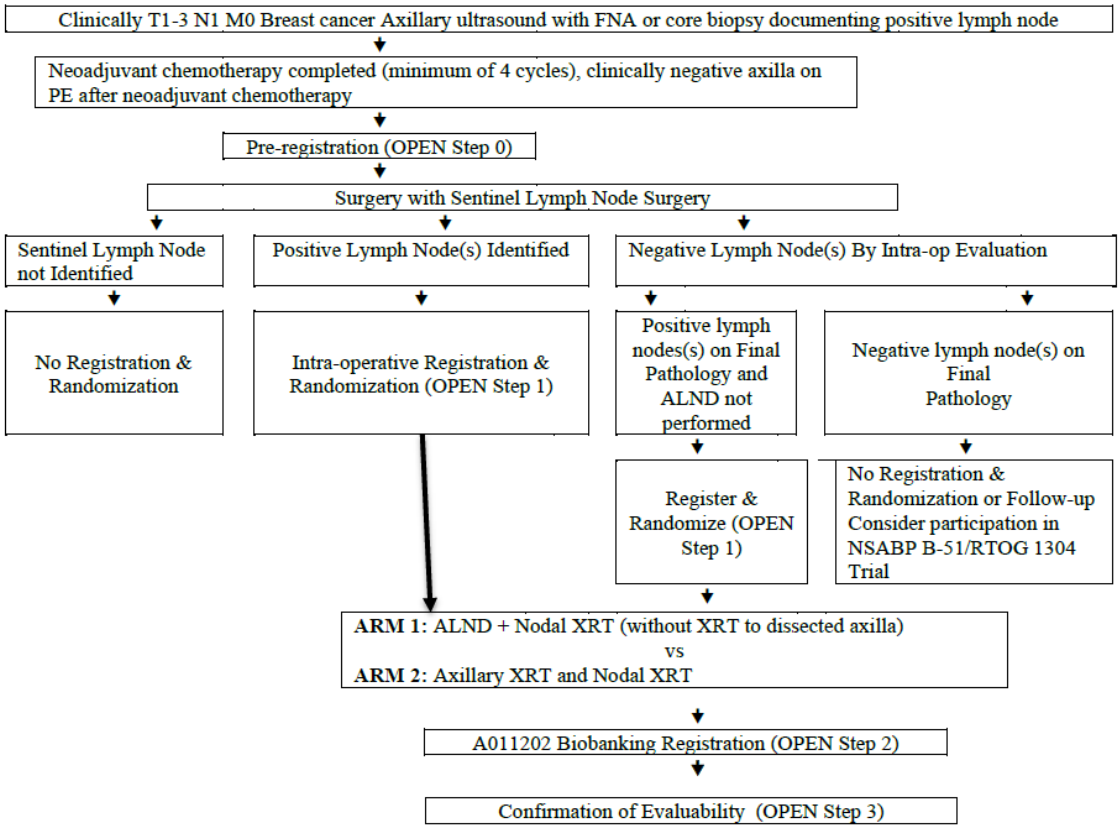
For cases where ALND has not been performed and one of the following is true: 1) intra-operative evaluation of sentinel lymph node could not be/was not performed and final pathology identified a positive lymph node (sentinel or non-sentinel) with metastasis greater than 0.2 mm. OR 2) lymph node (sentinel or non-sentinel) considered negative on intra-operative evaluation was found to be positive on final pathology (with metastasis greater than 0.2 mm).

1. Breast surgery (lumpectomy or mastectomy) and sentinel lymph node surgery must be completed within 112 days of the completion of the last dose of neoadjuvant chemotherapy. No additional chemotherapy and no radiation therapy are allowed in the intervening 112 days. Endocrine therapy or HER2-targeted therapy as a bridge between cytotoxic and surgical treatments are allowed. No experimental agents are allowed during this time.
   Negative margin (by either breast conservation or mastectomy) on final pathology where negative margin is defined as no tumor on ink. Patients may be registered and randomized with positive margins if there are plans to clear the margins prior to radiation therapy. Negative margins are

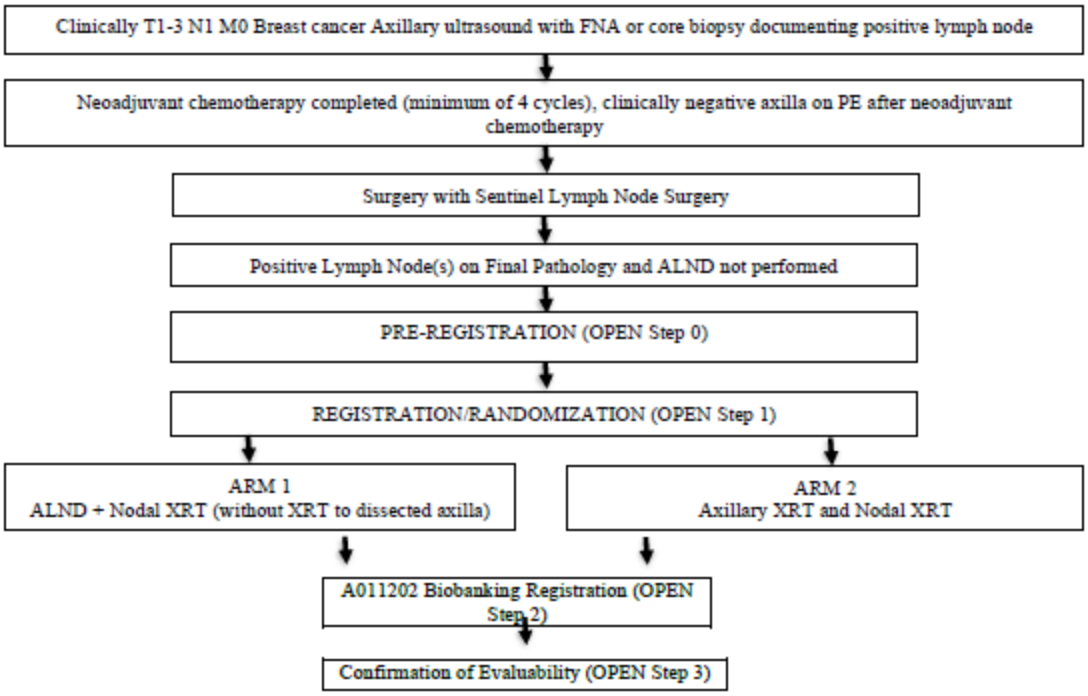
required prior to initiation of radiation therapy, and if not achieved, the patient should discontinue participation in the study (see Section 14.3.2).

2. At least one lymph node (sentinel or non-sentinel) with a metastasis greater than 0.2 mm in greatest dimension identified on final pathology (for cases where intra-operative evaluation was not performed, or was negative and completion dissection was not performed).
3. Among the minimum of 1 and the maximum of 6 nodes (sentinel + 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+).
4. For those patients who also undergo contralateral breast surgery, if invasive disease is found in the contralateral breast, the patient is not eligible for registration /randomization.

Schema for patients who pre-register prior to SLN surgery:



Schema for patients who pre-register AFTER surgery* (where SLN surgery was performed but ALND was NOT performed):



*** Patients who are pre-registered after SLN surgery are NOT eligible to enroll onto the Arm Lymphedema Companion Study (A011201-SI1)**