Cancer Research Consortium of West Michigan
P: 616.391.1230 | 800.336.6299 | www.crcwm.org

FAST FACTS

MA.39 - TAILOR RT: A RANDOMIZED TRIAL OF REGIONAL RADIOTHERAPY IN BIOMARKER LOW RISK NODE POSITIVE BREAST CANCER

Eligibility Criteria

1. Patients must be women with newly diagnosed histologically proven invasive carcinoma of the breast with no evidence of metastases, staged as per site standard of care.
2. Patients must have been treated by BCS or mastectomy with clear margins of excision*.
   * Patients treated by BCS with focally positive margins for invasive breast cancer or DCIS (involving < 3 high power fields) are eligible if additional surgery is not possible, e.g. posterior margin positive and deep resection margin abuts the chest wall or anterior margin positive and superficial resection margin abuts the skin. Boost radiotherapy must be administered for positive margins as described above.
   Post-mastectomy positive margins for invasive breast cancer and/or DCIS is not allowed.
   Multifocal disease (i.e. the presence of two or more foci of breast cancer within the same breast quadrant) and multicentric disease (i.e. the presence of two or more foci of breast cancer in different quadrants of the same breast) are allowed.
3. Patients with T3N0 disease are eligible.
4. Patients with disease limited to nodal micrometastases are eligible.
5. Patients with nodal *macrometastases (> 2 mm*) treated by axillary dissection must have 1-3 positive axillary nodes *(macrometastases, > 2 mm)*.*
6. Patients with nodal macrometastases (> 2 mm) treated by SLNB alone must have only 1-2 positive axillary nodes (macrometastases, > 2 mm)*.
   * Note patients with additional nodal micrometastases (> 0.2-2mm) or isolated tumour cells (≤ 0.2 mm) are eligible.

7. Patients must be ER ≥ 1% and HER2 negative on local testing
8. Patients must have an Oncotype DX recurrence score ≤ 25 obtained from testing of breast tumour tissue from a core biopsy or from the surgical specimen.**, ***
   ** If the patient does not already have Oncotype DX recurrence score, specimen (unstained blocks or slides) must be sent to the Genomic Health centralized laboratory in Redwood City, California. For Canadian sites, see the MA.39 website https://www.ctg.queensu.ca/trials/breast/ma39 and for US sites, see the CTSU website for the CCTG MA.39 trial for instructions on ordering Oncotype DX test.
   *** Oncotype DX testing must be performed on a core biopsy PRIOR to commencement of neoadjuvant endocrine therapy. See ineligibility criterion 3.2.8 for further details on the duration of neoadjuvant endocrine therapy.
9. Patient must consent to provision of, and investigator(s) must agree to submit to the CCTG Central Tumour Bank, a representative formalin fixed paraffin block of tumour tissue in order that the specific correlative marker assays described in the protocol may be conducted. Where tissue exists but local centre regulations prohibit submission of blocks of tumour tissue, the approval of the CCTG must be sought prior to randomization of the first patient to allow cores (two 2 mm cores of tumour from the block) and slides (20 x 5 micron thick unstained slides) of representative tumour tissue to be substituted. Where tumour tissue is available, failure to submit any tissue samples will result in the patient being considered ineligible.
10. Patient must consent to provision of samples of blood in order that the specific correlative marker assays described in the protocol may be conducted.

11. Patients must have had endocrine therapy initiated or planned for ≥ 5 years. Premenopausal women will receive ovarian ablation plus aromatase inhibitor therapy or tamoxifen if adjuvant chemotherapy was not administered. For all patients, endocrine therapy can be given concurrently or following RT.
12. Patients may or may not have had adjuvant chemotherapy.
13. RT must be administered within 16 weeks of definitive surgery if the patient is not treated with chemotherapy. If adjuvant chemotherapy is given, RT must begin within 12 weeks after the last dose. (Note: adjuvant chemotherapy may be ongoing at the time of randomization).
14. Patient's ECOG performance status must be 0, 1 or 2.
15. Patient's age must be ≥ 35 years.

16. For the first 736 eligible English or French-speaking subjects who have agreed to optional questionnaire completion: Patient is able (i.e. sufficiently fluent) and willing to complete the quality of life, health utilities and lost productivity questionnaires in either English or French. The baseline assessment must be completed within required timelines, prior to registration/randomization. Inability (lack of comprehension in English or French, or other equivalent reason such as cognitive issues or lack of competency) or refusal to complete the questionnaires will not make the patient ineligible for the study. Participation in questionnaire completion is mandatory for centres, but optional for patients.
17. Patient consent must be appropriately obtained in accordance with applicable local and regulatory requirements. Each patient must sign a consent form prior to enrollment in the trial to document their willingness to participate.
    A similar process must be followed for sites outside of Canada as per their respective cooperative group's procedures.
18. Patients must be accessible for treatment and follow-up. Investigators must assure themselves the patients randomized on this trial will be available for complete documentation of the treatment, adverse events, and follow-up.
19. In accordance with CCTG policy, protocol treatment is to begin within 3 weeks of patient randomization. Women of childbearing potential must have agreed to use an effective contraceptive method. A woman is considered to be of "childbearing potential" if she has had menses at any time in the preceding 12 consecutive months. In addition to routine contraceptive methods, "effective contraception" also includes heterosexual celibacy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy prevention) defined as a hysterectomy, bilateral oophorectomy or bilateral tubal ligation, or vasectomy/vasectomized partner. However, if at any point a previously celibate patient chooses to become heterosexually active during the time period for use of contraceptive measures outlined in the protocol, she is responsible for beginning contraceptive measures. Women of childbearing potential will have a pregnancy test to determine eligibility as part of the Pre-Study Evaluation (see Section 4.0); this may include an ultrasound to rule-out pregnancy if a false-positive is suspected. For example, when beta-human chorionic gonadotropin is high and partner is vasectomized, it may be associated with tumour production of hCG, as seen with some cancers. Patient will be considered eligible if an ultrasound is negative for pregnancy.

Ineligibility Criteria

Patients who fulfill any of the following criteria are not eligible for admission to the study:

1. Patients with nodal disease limited to isolated tumour cells ($pN0_{i+}$ < 0.2 mm).
2. Patients with pT3N1 and pT4 disease (Note: patients with T3N0 are eligible).
3. 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.)
4. Synchronous or previous contralateral invasive breast cancer. (Patients with contralateral DCIS are eligible unless previously treated with radiation.)
5. History of non-breast malignancies except adequately treated non-melanoma skin cancers, in situ cancers treated by local excision or other cancers curatively treated with no evidence of disease for ≥ 5 years.

6. Patients who are pregnant.
7. Patients that have had prior ipsilateral chestwall/thoracic radiation.
8. Patients treated with chemo or endocrine therapy administered in the neoadjuvant setting for breast cancer. Endocrine therapy exposure 12 weeks or less prior to surgery is permitted.
9. Patients with serious non-malignant disease (e.g. cardiovascular, scleroderma etc.) which would preclude RT.
10. Patients with any serious active or co-morbid medical conditions, laboratory abnormality, psychiatric illness, active or uncontrolled infections, or serious illnesses or medical conditions that would prevent the patient from participating or to be managed according to the protocol (according to investigator's decision).