Cancer Research Consortium of West Michigan
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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 have newly diagnosed histologically proven invasive carcinoma of the breast with no evidence of metastases.
2. Patients must have been treated by BCS or mastectomy.
3. Patients treated by BCS or mastectomy and axillary dissection must have 1-3 positive axillary nodes *(macrometastases, > 2 mm)*.*
4. Patients treated by BCS and SLNB alone must have only 1-2 positive axillary nodes *(macrometastases, > 2 mm)*.*
5. Patients treated by mastectomy and SLNB alone must have only 1 positive axillary node (*macrometastases, > 2 mm)*.*
   ** Note patients with additional nodal micrometastases (> 0.2-2mm) or isolated tumour cells (≤ 0.2 mm) are eligible. Patients with nodal disease limited only to micrometastases or isolated tumour cells are not eligible.*
6. Patients must be ER ≥ 1% and HER2 negative on local testing
7. Patients must have an Oncotype DX recurrence score <18**
   *** 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. Please see MA.39 trial specific website for instructions on ordering Oncotype DX test.*
8. Patient must consent to provision of, and investigator(s) must confirm access to and 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.
9. Patient must consent to provision of samples of blood in order that the specific correlative marker assays described in the protocol may be conducted.
10. Patients must have had endocrine therapy initiated or planned for ≥ 5 years. Endocrine therapy can be given concurrently or following RT
11. Patients may or may not have had adjuvant chemotherapy.
12. RT must be administered within 12 weeks of definitive surgery if the patient is not treated with chemotherapy. If adjuvant chemotherapy is given, RT must begin within 2-8 weeks after the last dose.
13. Patient's ECOG performance status must be 0, 1 or 2.
14. Patient's age must be ≥ 40 years.
15. Patient's life expectancy is ≥ 10 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

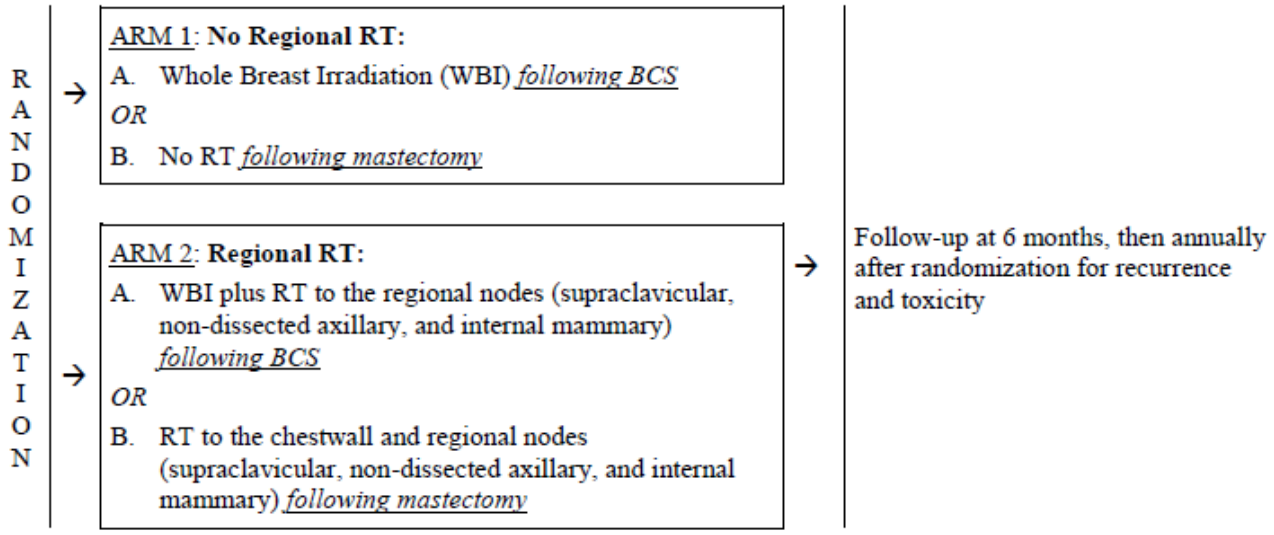
to complete the questionnaires will not make the patient ineligible for the study. Participation in questionnaire completion is mandatory for centres, but optional for patients.

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 micrometastases ($pN1M_i$, > 0.2 mm and ≤ 2 mm) or isolated tumour cells ($pN0_{i+}$ < 0.2 mm).
2. 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.)
3. Synchronous or previous contralateral invasive breast cancer. (Patients with contralateral DCIS not treated with radiation are eligible.)
4. 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.
5. Patients with pT3 or pT4 disease.
6. Patients who are pregnant.
7. Patients that have had prior ipsilateral chestwall/thoracic radiation.
8. Patients treated with neoadjuvant chemo or endocrine therapy for breast cancer.
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).



N = 2140 patients