Cancer Research Consortium of West Michigan
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# FAST FACTS

**NRG BR008:** A Phase III Randomized Trial of Radiotherapy Optimization for Low-Risk HER2-Positive Breast Cancer 'Her2 Radiation Optimization' (HERO)

**Eligibility Criteria**

***A patient cannot be considered eligible for this study unless ALL of the following conditions are met.***

**2.1.1** The patient or a legally authorized representative must provide study-specific informed consent prior to study entry and, for patients treated in the U.S., authorization permitting release of personal health information.

**2.1.2** The trial is open to female and male patients who have undergone **breast conserving surgery** and have completed neoadjuvant* or adjuvant systemic therapy with a HER2-targeted therapeutic regimen. While the standard duration of neoadjuvant or adjuvant systemic therapy is at least 12 weeks, patients will be eligible if they receive a minimum of 8 weeks of systemic therapy. Patients treated with T-DM1 must have received at least 6 cycles of this treatment.

*For the neoadjuvant cohort: Patients are eligible if they achieved pCR with HER2-targeted preoperative treatment. Patients treated with T-DM1 must have received at least 6 cycles of this treatment.

**2.1.3** The patient must be ≥ 18 years of age.

**2.1.4** The patient must have an ECOG performance status of 0 ,1, or 2/Karnofsky performance status above 60. (See Appendix A).

**2.1.5** Histologically or cytologically confirmed invasive breast carcinoma.

**2.1.6** The tumor must have been determined to be HER2-positive by current ASCO/CAP guidelines based on local testing results.

**2.1.7** The tumor must have ER and PgR status assessed locally using current ASCO/CAP Guidelines.

**2.1.8** Patient must have undergone axillary staging, either sentinel node biopsy (SNB) or axillary lymph nodal dissection (ALND). In neoadjuvant patients, SNB following

neoadjuvant therapy is strongly recommended. SNB prior to neoadjuvant therapy is discouraged, but patients are permitted if node negative (pN0).

**2.1.9** The following staging criteria must be met according to AJCC 8th edition criteria:

Adjuvant cohort

- By pathologic evaluation, the patient's primary tumor must be ? 3 cm and ipsilateral nodes must be pN0. Surgical lumpectomy margins must be negative for invasive cancer and ductal carcinoma in situ (no ink on tumor).

Neoadjuvant cohort

- Prior to neoadjuvant therapy, the patient's primary tumor must be ≤ 5 cm by imaging studies, with negative axillary nodes (cN0) based on axillary U/S, CT, PET or MRI. Physical examination is not sufficient documentation of cN0 status.
- Must be ypT0N0 at surgery (lumpectomy); patients with residual non-invasive disease (DCIS) in the surgical specimen (ypTis), are only eligible if residual DCIS spans ≤ 1 cm, and surgical margins are negative for DCIS.

**2.1.10** Bilateral mammogram or MRI within 52 weeks prior to randomization.

**2.1.11** HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months of randomization are eligible for this trial.

**Ineligibility Criteria**

***Patients with any of the following conditions are NOT eligible for this study.***

**2.1.12** Definitive clinical or radiologic evidence of metastatic disease.

**2.1.13** On the Adjuvant cohort, patients with a primary tumor > 3 cm on pathologic examination of the surgical specimen. On the Neoadjuvant cohort, patients with a primary tumor > 5 cm or with abnormal or suspicious ipsilateral axillary nodes by pretreatment imaging, unless demonstrated to be negative by cytologic or histologic examination.

**2.1.14** Pathologically positive axillary nodes at any time including of $pN0_{(i+)}$ or $pN0_{(mol+)}$ $ypN0_{(i+)}$ or $ypN0_{(mol+)}$ disease.

**2.1.15** Patient planning for or status-post mastectomy.

**2.1.16** Radiographically suspicious ipsilateral or contralateral axillary, supraclavicular, infraclavicular, or internal mammary lymph nodes, unless there is histological confirmation that these nodes are negative for metastatic disease.

**2.1.17** Suspicious microcalcifications, densities, or palpable abnormalities (in the ipsilateral or contralateral breast), or mass or non-mass enhancement on MRI (if performed) aside from the known cancer, unless biopsied and found to be benign.

**2.1.18** Non-epithelial breast malignancies such as sarcoma or lymphoma.

**2.1.19** Multicentric carcinoma (invasive cancer or DCIS) in more than one quadrant or multifocal disease spanning ≥ 4 centimeters. If multifocal, all foci should be confined to a maximum summed tumor extent of 3 cm determined by pathological assessment.

**2.1.20** Paget's disease of the nipple.

**2.1.21** Synchronous contralateral invasive breast cancer or DCIS or synchronous ipsilateral invasive breast cancer of a different histology. (Patients with synchronous and/or previous contralateral LCIS are eligible.)

**2.1.22** On the Adjuvant cohort, surgical margins that cannot be microscopically assessed or are positive at pathologic evaluation. (If surgical margins are rendered free of disease by re- excision, the patient is eligible).

**2.1.23** Treatment plan that includes regional nodal irradiation.

**2.1.24** Prior ipsilateral breast or thoracic RT for any condition (contralateral RT for DCIS ≥ 10 years prior to randomization is permitted).

**2.1.25** Patients treated for a prior invasive breast malignancy are excluded. Contralateral DCIS ≥ 10 years prior to enrollment is permissible.

**2.1.26** Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.

**2.1.27** Patients on oral, transdermal, or subdermal estrogen replacement (including all estrogen only and estrogen-progesterone formulas) are not eligible unless discontinued prior to randomization.

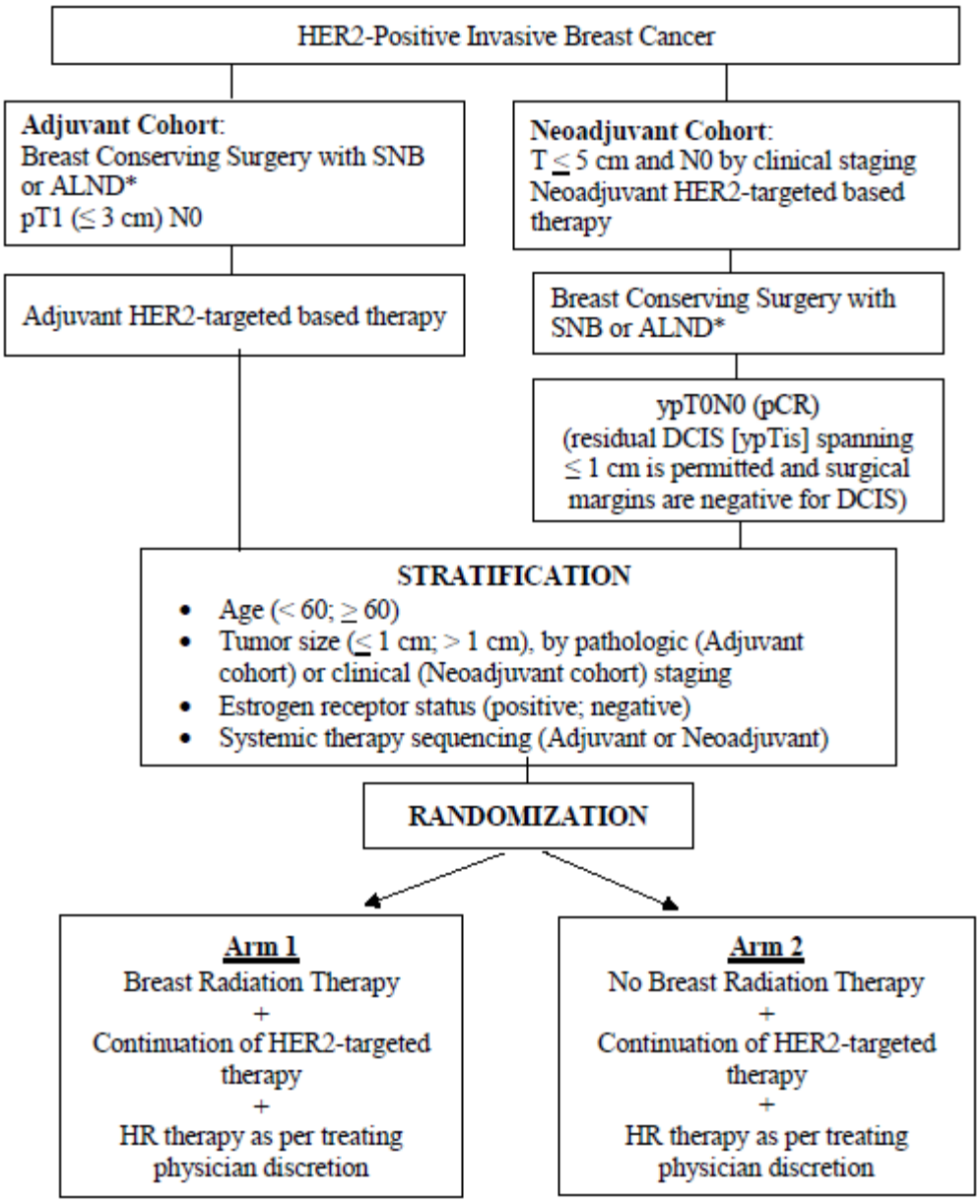
**2.1.28** Active collagen vascular disease, specifically dermatomyositis with a CPK level above normal or with an active systemic lupus erythematosus, or scleroderma.

**2.1.29** Clinicians should consider whether any conditions would make this protocol unreasonably hazardous for the patient.

**2.1.30** Pregnancy or lactation at the time of randomization or intention to become pregnant during treatment. ***(Note: Pregnancy testing according to institutional standards for patients of childbearing potential must be performed within 14 days prior to randomization.)***

**2.1.31** Use of any investigational product within 30 days prior to randomization.

Figure 1.
NRG-BR008 SCHEMA




*Sentinel node biopsy (SNB) or axillary lymph node dissection (ALND)