

FAST FACTS

S1703 - Randomized Non-Inferiority Trial Comparing Overall Survival of Patients Monitored With Serum Tumor Marker Directed Disease Monitoring (STMDDM) Versus Usual Care in Patients With Metastatic Hormone Receptor Positive HER-2 Negative Breast Cancer

Eligibility criteria

Disease Related Criteria

1. Patients must have a diagnosis of hormone receptor positive (ER+ and/or PR+), HER-2 negative, metastatic (M1) breast cancer and must be receiving or plan to receive first-line systemic treatment for metastatic disease. (Systemic treatment is any treatment meant to treat the whole body such as endocrine therapy +/- targeted therapy +/- chemotherapy).
NOTE: Participants are eligible if they have either de-novo metastatic breast cancer and/or recurrent breast cancer from an earlier stage that is now metastatic.
2. Patients must be registered to Step 1 between 14 days prior to and 60 days after start of first-line systemic treatment for metastatic disease.

Clinical/Laboratory Criteria

1. Patients (women and men) must be ≥ 18 years of age
2. Patients must have been tested for the following breast cancer specific STMs after diagnosis of metastatic disease and within ± 14 days of initiation of first-line systemic treatment for metastatic disease:
 - CEA (must be tested)
 - CA 15-3 or CA27.29 (at least one of these must be tested).At least one of the tested STMs must have been $\geq 2 \times$ the institutional upper limit of normal at this time. Testing all three STMs is encouraged but only two are required. Patients must plan to have the same two STMs tested for the duration that the patient is on protocol-specified disease monitoring.
3. Patients must have systemic radiographic imaging prior to initiation of systemic therapy or within 30 days of initiation of treatment for metastatic breast cancer and prior to Step 1 registration. Modality of imaging is at the discretion of the treating physician.
Note: the treating physician can order additional imaging tests at any point prior to randomization at their discretion.
4. Patients must be willing to obtain disease monitoring (imaging and/or serum tumor markers) from a consistent facility in which the registering site has access to the results for the duration of the study intervention (312 weeks after Step 2 randomization). Imaging and STMs do not need to be completed at the same facility.
5. Patients with known cirrhosis, untreated B12 deficiency, thalassemia, or sickle cell anemia are not eligible as these could cause falsely elevated STM levels.
6. Patients with known brain or leptomeningeal metastases are not eligible as they may require regular radiographic monitoring to assess treatment response.
7. Patients must not be currently enrolled or plan to participate in a first-line treatment trial for metastatic breast cancer with a defined monitoring schedule.

8. Patients who are able to complete questionnaires in English or Spanish must participate in patient-reported outcome (PRO) assessments as outlined in [Section 14.4](#).
9. Patients must not be pregnant due to the potential harm to the fetus from radiation exposure from radiographic imaging.
10. Except for breast cancer (and previous history of breast cancer), no other prior malignancy is allowed except for adequately treated basal (or squamous cell) skin cancer, *in situ* cervical cancer or other cancer for which the patient has been disease free for five years.

Prior/Concurrent Therapy Criteria

1. Patients must not have received prior systemic therapy for metastatic breast cancer, except for their current line of therapy.

Regulatory Criteria

1. Patients must have decision making capacity and be able to provide informed consent.
2. Patients **must** be informed of the investigational nature of this study and must sign and give written informed consent in accordance with institutional and federal guidelines. Use of legally-authorized representative is not permissible for this study.
3. As a part of the OPEN registration process (see Section 13.4 for OPEN access instructions) the treating institution's identity is provided in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.

STEP 2 RANDOMIZATION

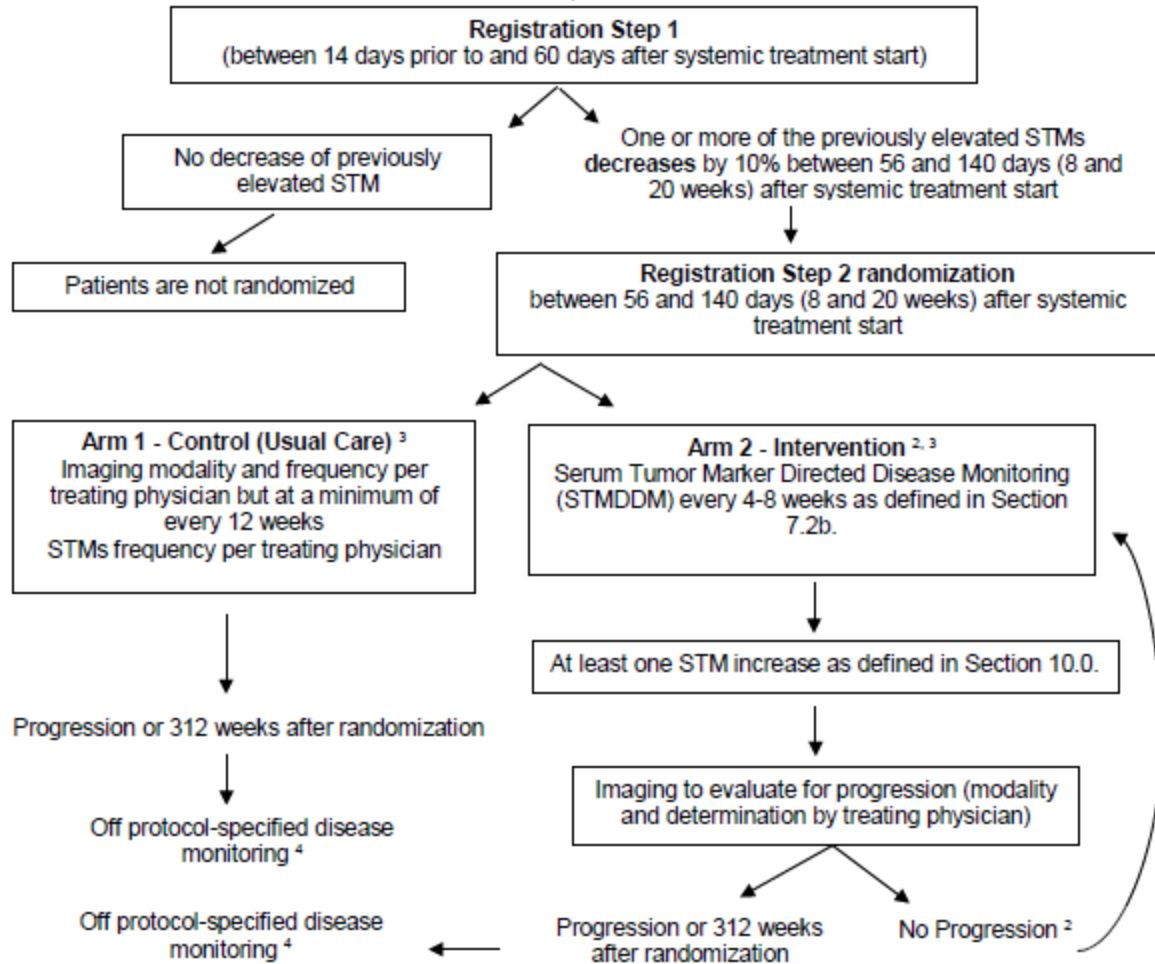
Clinical/Laboratory Criteria

1. Patients must be tested for the breast cancer specific STMs that were tested prior to Step 1 Registration (see Section 5.1d) between 56 and 140 days after initiation of first-line systemic therapy for metastatic disease:
 - CEA (must be tested)
 - CA 15-3 or CA 27.29 (whichever was tested prior to Step 1)
 Testing all three STMs is encouraged but only two are required. Patients must plan to have the same two STMs tested for the duration that the patient is on protocol-specified disease monitoring.
2. At least one of the STMs that was previously elevated must have decreased from the assessment at Step 1 by $\geq 10\%$ at this time. (See Section 10.0).
3. Patients must not have known progression since registration to Step 1.
4. Patients must be registered to Step 2 randomization between 56 days and 140 days after the initiation of first-line systemic therapy for metastatic disease. This window is inclusive; patients may be registered to Step 2 on Day 56 or on Day 140. Patients must have been eligible for Step 1 in order to be eligible for Step 2 Randomization.
5. Baseline questionnaires must be completed within 28 days prior to Step 2 randomization. (Note: Those patients who cannot complete the PRO questionnaires in English or Spanish can be registered to Step 2 without contributing to PRO research).

SCHEMA

Patients diagnosed with previously untreated metastatic HR⁺ HER-2 negative breast cancer undergoing or planning systemic treatment¹

One or more elevated breast cancer specific Serum Tumor Markers (STM) $\geq 2 \times$ IULN (after diagnosis and +/- 2 weeks of systemic treatment start for metastatic cancer)



¹ Participants are eligible if they have either de-novo metastatic breast cancer and/or recurrent breast cancer from an earlier stage that is now metastatic.
² If a patient develops new signs or symptoms concerning for disease progression, imaging may occur at that point in time, regardless of STM trend. If the treating physician does not confirm progression then STMDDM continues per protocol.
³ Patients will discontinue protocol-specified disease monitoring at the time of progression or 312 weeks after Step 2 Randomization, whichever comes first. All patients will be followed for vital status for 312 weeks from Step 2 randomization or until death, whichever comes first.
⁴ PRO and resource utilization data will continue to be collected through Week 102 on patients who progress or come off study for any reason. See Section 7.4.