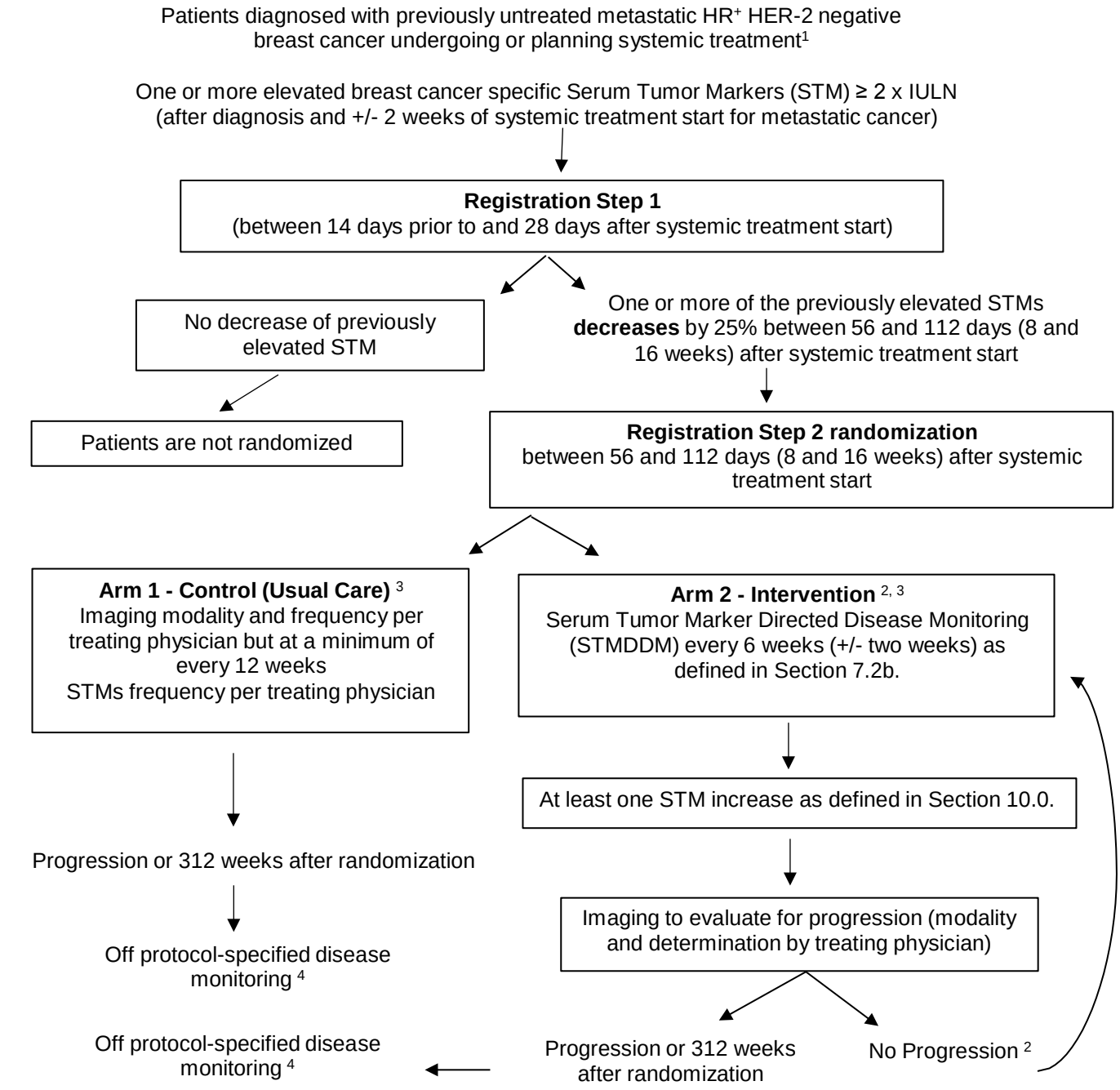
SCHEMA



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.

3.0 DRUG INFORMATION

There are no drugs used in this protocol.

4.0 STAGING CRITERIA

Note: All staging will be based on the American Joint Committee on Cancer 2010 Staging System, 7th Edition.

M1 Distant detectable metastases as determined by classical clinical and radiographic means and/or histologically proven larger than 0.2 mm.

5.0 ELIGIBILITY CRITERIA

Each of the criteria in the following section must be met in order for a patient to be considered eligible for registration. For each criterion requiring test results and dates, please record this information on the relevant Onstudy form and submit via Medidata Rave® (see Section 14.0). Any potential eligibility issues should be addressed to the SWOG Statistics and Data Management Center in Seattle at 206/652-2267 or cancercontrolquestion@crab.org prior to registration.

In calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test is done on a Monday, the Monday 2 weeks later would be considered Day 14. This allows for efficient patient scheduling without exceeding the guidelines. **If Day 14, 28, 56, or 112 falls on a weekend or holiday, the limit may be extended to the next working day.**

5.1 STEP 1 REGISTRATION

Disease Related Criteria

a. 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.

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.

b. Patients must be registered to Step 1 between 14 days prior to and 28 days after start of first-line systemic treatment for metastatic disease.

Clinical/Laboratory Criteria

c. Patients (women and men) must be ≥ 18 years of age

d. Patients must have been tested for all of 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:

- CA 15-3
- CA 27.29
- CEA

At least one of these STMs must have been ≥ 2 x the institutional upper limit of normal at this time

e. Patients must have systemic radiographic imaging prior to initiation of systemic therapy for treatment of metastatic breast cancer and prior to Step 1 registration with either:

- a computed tomography (CT) scan of the chest and abdomen with or without CT pelvis, and with or without bone scan

  or

- a positron emission tomography (PET) scan with or without CT

note: the treating physician can order additional imaging tests at any point prior to randomization at their discretion.

f. Patients must be willing to obtain disease monitoring (imaging and/or serum tumor markers) at their current center for the duration of the study intervention (312 weeks after Step 2 randomization).

g. Patients with known cirrhosis, untreated B12 deficiency, thalassemia, or sickle cell anemia are not eligible as these could cause falsely elevated STM levels.

h. Patients with known brain metastases are not eligible as they may require regular radiographic monitoring to assess treatment response.

i. 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.

j. 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.

k. Patients must not be pregnant due to the potential harm to the fetus from radiation exposure from radiographic imaging.

l. 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

m. Patients must not have received prior systemic therapy for metastatic breast cancer, except for their current treatment regimen initiated no more than 28 days prior to registration.

Regulatory Criteria

n. Patients must have decision making capacity and be able to provide informed consent.

o. 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.

p. As a part of the OPEN registration process (see Section 13.3 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.

5.2 STEP 2 RANDOMIZATION

Clinical/Laboratory Criteria

a. Patients must be tested for all of the following breast cancer specific STMs between 56 and 112 days after initiation of first-line systemic therapy for metastatic disease:

- CA 15-3
- CA 27.29
- CEA

b. At least one of the STMs that was previously elevated must have decreased from the assessment at Step 1 by ≥ 25% at this time. (See Section 10.0).

c. Patients must not have known progression since registration to Step 1.

d. Patients must be registered to Step 2 randomization between 56 days and 112 days after the initiation of first-line systemic therapy for metastatic disease. Patients must have been eligible for Step 1 in order to be eligible for Step 2 Randomization.

e. 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).

6.0 STRATIFICATION FACTORS

Patients will be randomized to Usual Care or Intervention (serum tumor marker directed disease monitoring) with stratification by bone only disease versus any visceral disease.