

FAST FACTS

S1501: PROSPECTIVE EVALUATION OF CARVEDILOL IN PREVENTION OF CARDIAC TOXICITY IN PATIENTS WITH METASTATIC HER-2+ BREAST CANCER, PHASE III

STEP 1 REGISTRATON

Disease Related Criteria

1. Patients must:

- a. Have metastatic breast cancer,
AND
- b. Be initiating within 11 calendar days of Step 1 Registration OR be continuing trastuzumab-based HER-2 targeted therapy without concurrent anthracyclines,
AND
- c. Be receiving the trastuzumab-based HER-2 targeted therapy in first or second line setting.

Patients may have brain metastasis. There is no limit for number of doses of HER-2 targeted therapy prior to registration.

Examples of eligible HER-2 targeted therapy:

- Trastuzumab
- Trastuzumab + chemotherapy or hormonal therapy
- Trastuzumab + other HER-2 targeted agent with or without chemotherapy (such as pertuzumab)
- Ado-trastuzumab (Kadcyla®)

NOTE: Patients on lapatinib without trastuzumab are not eligible. Planned treatment with concurrent HER-2 targeted therapy and anthracyclines is not permitted.

Prior/Concurrent Therapy Criteria

1. Patients must be at increased risk for cardiotoxicity defined by at least one of the following:
 - a. Previous anthracycline exposure
OR
 - b. 1 or more of the following risk factors for heart disease:
 - LVEF 50-54% by local ECHO read
 - Age \geq 65
 - BMI \geq 30 kg/m²
 - Current or prior anti-hypertensive therapy
 - Diagnosis of coronary artery disease (CAD)
 - Diagnosis of diabetes mellitus
 - Diagnosis of atrial fibrillation/flutter
2. Patients must not have taken within 21 days prior to Step 1 Registration, be currently taking at the time of Step 1 Registration, or planning to take once registered to Step 1 a beta blocker, ARB, or ACE inhibitor in order to be randomized (Arms 1 and 2).

Patients currently taking a beta blocker, ARB, or ACE inhibitor at the time of Step 1 Registration are eligible to register for the non-randomized observational cohort (Arm 3).

3. Patients must not be currently taking or planning to take the following medications during study treatment or observation:
 - B2 agonists
 - Bosutinib
 - Ceritinib
 - Floctafenine
 - Methacholine
 - Pazopanib
 - Rivastigmine
 - Vincristine
 - Silodosin

Clinical/Laboratory Criteria

1. Patients must have a Zubrod Performance Status of 0-2. (see [Section 10.7](#)).
2. Patients must be ≥ 18 years of age.
3. Patients must have a complete physical examination and medical history within 28 days prior to registration.
4. Patients must have LVEF $\geq 50\%$ by 2-D echocardiogram within 28 days prior to registration. The echocardiogram must be obtained from the site's approved **S1501** Validated ECHO Lab and submitted for central review by the **S1501** ECHO Core Lab (see [Section 15.2](#)). An ECHO should not be submitted for central read until patient has been registered.
5. Patients must have adequate hepatic function as evidenced by all of the following within 28 days prior to registration: serum bilirubin $< 3.0 \times$ institutional upper limit of normal (IULN), SGOT/AST and SGPT/ALT $< 5.0 \times$ IULN.
6. Patients must have a systolic blood pressure ≥ 80 mm Hg within 14 days prior to registration. (See Section 9.1 and 9.2, Footnote B.)
NOTE: Patients enrolled at sites in Korea must have a systolic blood pressure ≥ 90 mm Hg within 14 days prior to registration.
7. Patients must have a systolic blood pressure ≥ 80 mm Hg within 14 days prior to registration.
8. Patients must not be dialysis dependent.
9. Patients must not have uncontrolled asthma. Patients may use a steroid inhaler or other treatment, but patients must not require use of B2 agonists more than once weekly.
10. Patients must not have uncontrolled asthma.
11. Patients must not co-enroll on other treatment trials.
12. No other prior malignancy is allowed except for the following: adequately treated basal cell or squamous cell skin cancer, in situ cervical cancer, prostate cancer on active surveillance, adequately treated Stage I or II cancer from which the patient is currently in complete remission, or any other cancer from which the patient has been disease free for five years.
13. Patients must not be pregnant or nursing due to potential fetal or nursing infant harm. Women/men of reproductive potential must have agreed to use an effective contraceptive method. A woman is considered to be of "reproductive 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. 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, he/she is responsible for beginning contraceptive measures.

Specimen Submission Criteria

1. Patients must be willing to submit blood specimens as outlined in Section 15.1.

2. Sites must seek additional patient consent for the future use of specimens as described in Section 15.0.

STEP 2 REGISTRATION (Randomization)

- a. Patients must not be registered to Step 2 until confirming via RAVE EDC that the patient's LVEF by echocardiogram was $\geq 50\%$ by central review. Patients must be registered within 11 calendar days of submission of the ECHO study.
- b. Site must verify that there is no known change in the Step 1 eligibility since initial registration.

SCHEMA

METASTATIC HER-2+ BREAST CANCER WITH CURRENT OR PLANNED HER-2 TARGETED THERAPY INCLUDING TRASTUZUMAB

