# Clinical Trials Data ERBB2 - Document 59

# Phase II Study of Eribulin Mesylate, Trastuzumab, and Pertuzumab in Women With Metastatic, Unresectable Locally Advanced, or Locally Recurrent HER2-Positive Breast Cancer

## Clinical Trial: https://clinicaltrials.gov/study/NCT01912963

"eligibilityCriteria": "Inclusion Criteria:\n\nParticipants must meet the following criteria on screening examination to be eligible to participate in the study:\n\n- Participants must have invasive primary tumor or metastatic tissue confirmation of human epidermal growth factor receptor 2 (HER2)-positive status, defined as presence of one or more of the following criteria: Over-expression by immunohistochemistry (IHC) with score of 3+ AND/OR HER2 gene amplification (\\> 6 HER2 gene copies per nucleus or a FISH ratio \\[HER2 gene copies to chromosome 17 signals\\] of \u2265 2.0) Note: Participants with a negative or equivocal overall result (FISH ratio of \\<2.0 or \u2264 6.0 HER2 gene copies per nucleus) and IHC staining scores of 0, 1+, 2+ are not eligible for enrollment.\n\n\* Participants must have metastatic, unresectable locally advanced, or locally recurrent HER2-positive breast cancer. For the phase II portion of the study, it is required that participants have measurable disease, as defined by RECIST 1.1, which can be accurately evaluated on computerized tomography (CT) or magnetic resonance (MRI). Measurable disease is defined as: at least one lesion of \\>10 mm in the longest diameter for a non-lymph node or \\>15 mm in the short-axis diameter for a lymph node which is serially measurable according to RECIST 1.1.criteria.1\n\* Participants must have received at least 1 line of chemotherapy for advanced or metastatic breast cancer and/or relapse/progressed while on or within 6 months of completion of neoadjuvant or adjuvant trastuzumab. Prior pertuzumab is allowed in the phase II portion of the trial.\n\* Participants must have had prior trastuzumab therapy (either in the adjuvant or metastatic setting).\n\* Participants must be at least 2 weeks out from prior endocrine therapy, chemotherapy,radiotherapy, or other cancer-directed therapy (including novel agents), with adequate recovery of toxicity to baseline, or grade \u22641, with the exception of alopecia and hot flashes. Participants may have initiated bisphosphonate/denosumab therapy prior to start of protocol therapy. Biphosphonate/denosumab therapy may continue during protocol treatment. Such participants will have bone lesions considered evaluable for progression. Washout for trastuzumab is not necessary.\n\* Women and men, age 18 years at the time of informed consent.\n\* Participants must have an Eastern Cooperative Oncology Group (ECOG) performance status 0-1 or a Karnofsky Performance Scale (KP) 70%.\n\* Participants must have normal organ and marrow function as defined below:\n\* Absolute neutrophil count \\> 1,500/mcL\n\* Platelets \\> 75,000/mcL\n\* Hemoglobin \\>9g/dl\n\* Total bilirubin \u22642.0 X institutional upper limit of normal\n\* Aspartate Aminotransferase (AST, SGOT)/ALT(Alanine Aminotransferase, SGPT) \u2264 3 X institutional ULN without liver metastases, or \u2264 5 times institutional upper limit normal (ULN) with liver metastases (if liver metastases felt to be cause of Liver function tests (LFT) abnormalities)\n\* Alkaline phosphatase (ALP) \u22643 x institutional upper limit of normal If total ALP is \\>3x institutional upper limit normal (in the absence of liver metastasis) or \\>5x institutional upper limit of normal (in subjects with liver metastasis) AND the subject is known to have bone metastases, then liver ALP isoenzyme should be used to assess liver function rather than total ALP.\n\* Creatinine 2.0 mg/dL or creatinine clearance \u226550 mL/min.\n\* left ventricular ejection fraction (LVEF) \u226550%, as determined by radionucleoventilugrams (RVG) (multi-gated acquisition-MUGA) or Echocardiogram (ECHO) within 60 days prior to initiation of protocol therapy.\n\* Adequate IV access\n\* The effects of eribulin mesylate, trastuzumab, and pertuzumab on the developing human fetus are unknown. Pre-clinical data was suggestive of a teratogenic effect of eribulin mesylate. Pertuzumab caused oligohydramnios, delayed renal development and embryo-fetal deaths in pregnant cynomolgus monkeys. In the post-marketing setting, cases of oligohydramnios, some associated with fatal pulmonary hypoplasia of the fetus have been reported in pregnant women receiving trastuzumab. For these reasons women of child bearing potential and men must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) prior to study entry and for the duration of study participation. Should a woman become pregnant or suspect she is pregnant while participating in this study, she should inform her treating physician immediately.\n\* Ability to understand and willingness to sign a written informed consent document (approved by Institutional review board or independent ethics committee) obtained prior to any study procedure, with the understanding that the subject may withdraw at any time without prejudice.\n\* Laboratory tests required for eligibility must be completed within 14 days prior study entry. Baseline tumor measurements must be documented from tests within 28 days of study entry. Other non-laboratory tests must be performed within 28 days of study entry.\n\* For the Phase 2 portion of the study; patients must have tissue that is amenable to biopsy and must be willing to undergo research biopsy.\n\nExclusion Criteria: - Participants who exhibit any of the following conditions at screening will not be eligible for admission into the study:\n\n\* Participants receiving any other study agents.\n\* Participants receiving any other cancer directed concurrent therapy; such as concurrent chemotherapy, radiotherapy, or hormonal therapy. Concurrent treatment with biphosphonates/denosumab is allowed but should be started before starting treatment on study.\n\* Active brain metastases: Participants with previously diagnosed brain metastases are eligible if they have completed treatment at least one month prior to enrollment, are neurologically stable, and have recovery from effects of radiotherapy or surgery.\n\* History of allergic reaction attributed to compounds of similar chemical or biologic composition to eribulin mesylate, trastuzumab or pertuzumab, which cannot be managed by premedication.\n\* Participants who previously received eribulin mesylate are not eligible for enrollment on the phase II portion.\n\* Prior chemotherapy, targeted therapy, hormonal therapy, or radiation therapy (including any investigational agents) within 2 weeks prior entering the study or those who have not recovered adequately from adverse events (AEs) due to agents administered more than 4 weeks earlier (excluding alopecia and hot flashes). A washout period is not necessary for trastuzumab (or pertuzumab for run-in patients when applicable).\n\* A baseline corrected QT interval of \\> 470 ms.\n\* Pre-existing neuropathy \u2265 grade 2 (NCI Common Toxicity Criteria for Adverse Events (CTCAE) Version 4.0)\n\* Uncontrolled intercurrent illness including, not limited to ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements or other significant diseases or disorders that, in the investigator's opinion, would exclude the subject from participating in the study\n\* Symptomatic intrinsic lung disease or extensive tumor involvement of the lungs, resulting in grade 2 or higher dyspnea at rest.\n\* Currently pregnant or breast-feeding. All females must have a negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of \u03b2-Human Chorionic Gonadotropin (\u03b2-Hcg) at the Baseline visit \\[within 7 days of the first dose of study treatment\\]). Females of childbearing potential must agree to use a medically acceptable method of contraception (e.g., abstinence, an intrauterine device, a double-barrier method such as condom + spermicidal or condom + diaphragm with spermicidal, a contraceptive implant, an oral contraceptive or have a vasectomized partner with confirmed azoospermia) throughout the entire study period and for 30 days after discontinuation of study treatment. The only subjects who will be exempt from this requirement are postmenopausal women (defined as women who have been amenorrheic for at least 12 consecutive months, in the appropriate age group, without other known or suspected primary cause) or subjects who have been sterilized surgically or who are otherwise proven sterile (i.e., bilateral tubal ligation with surgery at least 1 month before start of study treatment, hysterectomy, or bilateral oophorectomy with surgery at least 1 month before start of study treatment). Current, ongoing protocols containing pertuzumab have included continuous pregnancy monitoring during the trial and for six months after the last dose of study drug is administered. Because of the long half-life of pertuzumab, women should be warned not to become pregnant for at least six months after completion of treatment.\n\* Individuals with a history of different malignancy are ineligible except for the following circumstances. Individuals with a history of other malignancies are eligible if they have been disease-free for at least 5 years and are deemed by the investigator to be at low risk for recurrence of that malignancy. Individuals with the following cancers are eligible if diagnosed and treated within the past 5 years: cervical cancer in situ, and non-melanoma cancer of the skin.",  
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"OLDER\_ADULT"  
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Question:  
Based on the following clinical trial information, would a patient with a ERBB2 gene mutation be eligible for the clinical trial?

Answer:  
This trial requires HER2-positive breast cancer, defined as either:  
  
\* \*\*IHC score of 3+\*\* \*\*AND/OR\*\*  
\* \*\*HER2 gene amplification\*\* ( > 6 HER2 gene copies per nucleus OR FISH ratio ≥ 2.0).  
  
Just having an ERBB2 (which is the gene that codes for HER2) mutation isn't enough information. The trial specifically requires HER2 \*overexpression\* or \*amplification\* to be considered HER2-positive. A patient could have an ERBB2 mutation without meeting these overexpression/amplification criteria.  
  
Therefore, based on this information alone, we \*\*cannot determine\*\* if a patient with an ERBB2 gene mutation would be eligible. They would need to have testing done (IHC and/or FISH) to determine their HER2 status according to the trial's specific definition.