# Clinical Trials Data ERBB2 - Document 57

# HER2-positive Breast Cancer With Brain Metastasis (GCC 1345)

## Clinical Trial: https://clinicaltrials.gov/study/NCT01924351

"eligibilityCriteria": "Inclusion Criteria:\n\n\* Histologically proven diagnosis HER2-positive breast cancer. Her2-positive is defined as follows:\n\n \\\* Validated IHC assay score of 3+ (defined as uniform, intense staining of \\>30% of invasive tumor cells)\n\* OR- Average HER2 gene copy number of \\>6\n\* OR- Gene amplified (HER2:D17Z1 ratio \\>2.20).\n\* Patients with 1-10 newly diagnosed brain metastases\n\* The contrast-enhancing intraparenchymal brain tumor must be well circumscribed and must have a maximum diameter of \u2264 4.0 cm in any direction on the enhanced scan. If multiple lesions are present and one lesion is at the maximum diameter, the other(s) must not exceed 3.0 cm in maximum diameter.\n\* History and physical with neurological examination, steroid documentation, height, and weight within 14 days of registration.\n\* A diagnostic contrast-enhanced MRI of the brain must be performed within 28 days prior to registration.\n\* Eligibility for treatment with SRS confirmed by a radiation oncologist.\n\* Performance Status 0-2\n\* Age \u2265 18.\n\* CBC with differential obtained within 14 days prior to registration, with adequate bone marrow function defined as follows:\n\* Absolute neutrophil count (ANC) \u2265 1,100 cells/mm3.\n\* Platelets \u2265 75,000 cells/mm3.\n\* Hemoglobin \u2265 9.0 g/dl (Note: The use of transfusion or other intervention to achieve Hgb \u22659.0 g/dl is acceptable).\n\* Adequate renal function within 14 days prior to registration, as defined below:\n\* BUN \u2264 30 mg/dl.\n\* Creatinine \u2264 1.5 x ULN\n\* Creatinine clearance \u226530 mL/min.\n\nAdequate hepatic function within 14 days prior to registration, as defined below:\n\n\* Total Bilirubin \u22641.5 x ULN\n\* ALT/AST \u2264 2.5 x upper limit of normal (ULN).\n\* Systolic blood pressure \u2264 160 mg Hg or diastolic pressure \u2264 90 mg Hg within 14 days prior to registration.\n\* Prothrombin time/international normalized ratio (PT INR) \\< 1.4 for patients not on warfarin confirmed by testing within 14 days prior to registration. Patients on full-dose anticoagulants (e.g., warfarin or LMW heparin) must meet both of the following criteria:\n\* No active bleeding or pathological condition that carries a high risk of bleeding (e.g., tumor involving major vessels or known varices).\n\* In-range INR (between 2.5 and 3.5) on a stable dose of warfarin-based oral anticoagulant; or on a stable dose of low molecular weight heparin; or INR between 1.5 and 2 if a Greenfield filter is in place.\n\* Patient must provide study specific informed consent prior to study entry.\n\* For women of child-bearing potential, negative serum pregnancy test within 14 days prior to registration.\n\* Women of childbearing potential and male participants must practice adequate contraception.\n\* Echocardiogram or MUGA scan with ejection fraction within normal institution limits within 28 days of registration\n\nExclusion Criteria:\n\n\* Prior invasive malignancy (except for non-melanomatous skin cancer) unless disease free for \u2265 3 years. For example, carcinoma in situ of the oral cavity and cervix are all permissible.\n\* Leptomeningeal metastases\n\* Previous treatment with all of the following: lapatinib, trastuzumab, pertuzumab, and trastuzumab emtansine. (Patients are eligible if treated with 3 or less of these agents.)\n\* Prior cranial radiotherapy.\n\* Prior resection of cerebral metastases\n\* Allergy to gadolinium\n\nSevere, active co-morbidity, defined as follows:\n\n\* Unstable angina and/or congestive heart failure within the last 6 months.\n\* Transmural myocardial infarction within the last 6 months.\n\* New York Heart Association grade II or greater congestive heart failure requiring hospitalization within 12 months prior to registration.\n\* History of stroke, cerebral vascular accident (CVA) or transient ischemic attack within 6 months.\n\* Serious and inadequately controlled cardiac arrhythmia.\n\* Significant vascular disease (e.g., aortic aneurysm, history of aortic dissection) or clinically significant peripheral vascular disease.\n\* Evidence of bleeding diathesis or coagulopathy.\n\* Serious or non-healing wound, ulcer, or bone fracture or history of abdominal fistula, gastrointestinal perforation or intra-abdominal abscess, major surgical procedure or significant traumatic injury within 28 days prior to registration, with the exception of the craniotomy for tumor resection or follow-on craniotomies to manage complications of brain tumor management such as hemorrhage or infection.\n\* Bacterial or fungal infection requiring intravenous antibiotics at the time of registration.\n\* Chronic obstructive pulmonary disease exacerbation or other respiratory illness requiring hospitalization or precluding study therapy at the time of registration.\n\* Hepatic insufficiency resulting in clinical jaundice and/or coagulation defects; note, however, that laboratory tests for coagulation parameters are not required for entry into this protocol.\n\* Active connective tissue disorders, such as lupus or scleroderma, that in the opinion of the treating physician may put the patient at high risk for radiation toxicity.\n\* Any other major medical illnesses or psychiatric impairments that in the investigator's opinion will prevent administration or completion of protocol therapy.\n\* Cognitive impairment that precludes a patient from acting as his or her own agent to provide informed consent.\n\* Women of childbearing potential who are sexually active and not willing/able to use medically acceptable forms of contraception; this exclusion is necessary because the chemotherapeutic treatment involved in this study is potentially teratogenic.\n\* Pregnant or lactating women, due to possible adverse effects on the developing fetus or infant due to study treatment.\n\* Patients treated on any other therapeutic clinical protocols within 30 days prior to study entry or during participation in the study.\n\* Inability to undergo MRI (e.g., due to safety reasons, such as presence of a pacemaker).\n\* Inability to undergo SRS due to claustrophobia",  
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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:  
The eligibility criteria mention "HER2-positive breast cancer" and define it by IHC score, HER2 gene copy number, and HER2:D17Z1 ratio. While an ERBB2 mutation can lead to HER2-positive breast cancer, simply having the mutation isn't enough for automatic inclusion.   
  
The trial requires confirmation of HER2 \*overexpression\*, not just the presence of the mutation. The patient needs to meet \*one\* of the following HER2-positive criteria:  
  
\* \*\*IHC score of 3+:\*\* This is a measure of protein overexpression.  
\* \*\*Average HER2 gene copy number of >6:\*\* This measures gene amplification.  
\* \*\*HER2:D17Z1 ratio >2.20:\*\* This also indicates gene amplification.  
  
Therefore, a patient with an ERBB2 mutation would be eligible for this trial \*only if\* they also meet one of the above HER2-positive criteria as determined by appropriate testing. The presence of the ERBB2 mutation alone is insufficient for eligibility.