# Clinical Trials Data ERBB2 - Document 15

# Safety and Efficacy Study of Sapanisertib in Combination With Exemestane or Fulvestrant in Postmenopausal Women With Estrogen Receptor Positive/Human Epidermal Growth Factor Receptor 2 Negative (ER+/HER2-) Metastatic Breast Cancer

## Clinical Trial: https://clinicaltrials.gov/study/NCT02049957

"eligibilityCriteria": "Inclusion Criteria\n\nEach patient must meet all of the following inclusion criteria to be enrolled in the study:\n\nPhase 1b and Phase 2\n\n1. Advanced or metastatic breast cancer.\n2. Histological or cytological confirmation of ER+ status (defined as \\> 1% positive tumor cells), and histological or cytological confirmation of HER2-negative (HER2-) status by local laboratory testing using criteria in the American Society of Oncology (ASCO)/College of American Pathologists (CAP) Clinical Practice Guideline update.\n3. Female patients 18 years of age or older who are postmenopausal for at least 1 year before the Screening visit, where menopause is defined by: Age \u2265 55 years and 1 year or more of amenorrhea. Surgical menopause with bilateral oophorectomy\n\n Age \\< 55 years and 1 year or more of amenorrhea, with an estradiol assay \\< 20 pg/mL\n\n Note: Ovarian radiation or treatment with a luteinizing hormone-releasing hormone agonist (goserelin acetate or leuprolide acetate) is not permitted for induction of ovarian suppression.\n4. Have a history of brain metastasis are eligible for the study provided that all the following criteria are met:\n\n Brain metastases which have been treated\n \* No evidence of disease progression for \u2265 3 months or hemorrhage after treatment\n \* Off-treatment with dexamethasone for 4 weeks before administration of the first dose of MLN0128\n \* No ongoing requirement for dexamethasone or anti-epileptic drugs\n5. Eastern Cooperative Oncology Group (ECOG) performance status 0 to 2.\n6. Clinical laboratory values as specified below within 4 weeks before the first dose of MLN0128:\n\n \* Bone marrow reserve consistent with absolute neutrophil count (ANC) \u2265 1.5 x 10\\^9/L; platelet count \u2265 100 x 10\\^9/L; hemoglobin \u2265 9 g/dL\n \* Total bilirubin \u2264 1.5 x the upper limit of the normal range (ULN), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) \u2264 2.5 x ULN (\u2264 5 x ULN if liver metastases are present)\n \* Creatinine clearance \u2265 50 mL/min based either on Cockcroft-Gault estimate or based on a 12- or 24-hour urine collection\n \* Fasting serum glucose \u2264 130 mg/dL and fasting triglycerides \u2264 300 mg/dL\n7. Left ventricular ejection fraction (LVEF) within 5 absolute percentage points of institutional standard of normal as measured by echocardiogram (ECHO) or multiple gated acquisition scan (MUGA) within 4 weeks before the first dose of MLN0128 (ie, if the institutional standard of normal is 50%, LVEF may be as low as 45% to be eligible for the study).\n8. Able to provide paraffin blocks or a minimum of 10 unstained slides of available archival tumor tissues (paraffin blocks are preferred). If archival tumor tissue is not available, a tumor biopsy may be performed before the patient begins treatment with MLN0128. If fewer than 10 slides are available or the tumor content/area requirements are not met, study eligibility will be determined upon discussion with the sponsor.\n9. Ability to swallow oral medications, willingness to perform mucositis prophylaxis, and suitable venous access for the study-required blood sampling.\n10. Voluntary written consent must be given before the performance of any study related procedure not part of standard medical care, with the understanding that consent may be withdrawn by the patient at any time without prejudice to future medical care.\n\n Phase 1b Only: In addition to the previously mentioned inclusion criteria, each patient must meet the following inclusion criterion to be enrolled in the phase 1b portion of the study:\n11. Patients may have SD or disease progression during their most recent treatment with exemestane or fulvestrant, or everolimus in combination with either exemestane (any country) or fulvestrant (US only). Exemestane or fulvestrant in combination with MLN0128 can also be initiated as a new line of therapy.\n\n Phase 2 Only: In addition to the previously mentioned inclusion criteria, each patient must meet all of the following inclusion criteria to be enrolled in the phase 2 portion of the study:\n12. Measurable disease defined as follows:\n\n \* At least 1 extra-osseous lesion that can be accurately measured in at least 1 dimension. The lesion must measure \u2265 20 mm with conventional imaging techniques or \u2265 10 mm with spiral computed tomography (CT) or magnetic resonance imaging (MRI), or\n \* Bone lesions (lytic or mixed \\[lytic plus sclerotic\\]) in the absence of measurable disease as defined above\n13. Patients must have had disease progression during treatment with everolimus in combination with either exemestane (any country) or fulvestrant (US only) (duration of treatment \u2265 4 weeks) and must have tolerated everolimus treatment in combination with exemestane (any country) or fulvestrant (US only) adequately according to the treating physician's judgment. Everolimus in combination with exemestane or fulvestrant is not required to be the most recent treatment before enrollment, but progression on the most recent anticancer therapy is required for enrollment.\n\nExclusion Criteria\n\nPatients meeting any of the following exclusion criteria are not to be enrolled in the study:\n\nPhase 1b and Phase 2\n\n1. Prior anticancer therapy or other investigational therapy within 2 weeks before administration of the first dose of MLN0128 (except for exemestane or fulvestrant, which should be continued). Treatment with everolimus must be discontinued 2 weeks before administration of the first dose of MLN0128.\n2. Chronic concomitant therapy with bisphosphonates or denosumab for the prevention of bone metastases. Concomitant treatment with bisphosphonates or denosumab is permitted for treatment of osteoporosis or management of existing bone metastases if initiated at least 4 weeks before administration of the first dose of MLN0128.\n3. Initiation of treatment with hematopoietic growth factors, transfusions of blood and blood products, or systemic corticosteroids (either IV or oral steroids, excluding inhalers) within 1 week before administration of the first dose of MLN0128 (patients already receiving erythropoietin on a chronic basis for \u2265 4 weeks are eligible).\n4. Previous treatment with dual PI3K/mTOR inhibitors or TORC1/2 inhibitors.\n5. Manifestations of malabsorption due to prior gastrointestinal (GI) surgery, GI disease, or for an unknown reason that may alter the absorption of MLN0128.\n6. Poorly controlled diabetes mellitus defined as glycosylated hemoglobin (HbA1c) \\> 7%; patients with a history of transient glucose intolerance due to corticosteroid administration may be enrolled in this study if all other inclusion/exclusion criteria are met.\n7. Other clinically significant co-morbidities, such as uncontrolled pulmonary disease, active central nervous system disease, active infection, or any other condition that could compromise participation of the patient in the study.\n8. Known human immunodeficiency virus infection.\n9. History of any of the following within the last 6 months before administration of the first dose of MLN0128:\n\n \* Ischemic myocardial event, including angina requiring therapy and artery revascularization procedures\n \* Ischemic cerebrovascular event, including transient ischemic attack and artery revascularization procedures\n \* Requirement for inotropic support (excluding digoxin) or serious (uncontrolled) cardiac arrhythmia (including atrial flutter/fibrillation, ventricular fibrillation, or ventricular tachycardia)\n \* Placement of a pacemaker for control of rhythm\n \* New York Heart Association Class III or IV heart failure\n \* Pulmonary embolism\n10. Significant active cardiovascular or pulmonary disease before administration of the first dose of MLN0128, including:\n\n \* Uncontrolled hypertension (ie, systolic blood pressure \\> 180 mm Hg; diastolic blood pressure \\> 95 mm Hg)\n \* Pulmonary hypertension\n \* Uncontrolled asthma or oxygen saturation \\< 90% by arterial blood gas analysis or pulse oximetry on room air\n \* Significant valvular disease; severe regurgitation or stenosis by imaging independent of symptom control with medical intervention; or history of valve replacement\n \* Medically significant (symptomatic) bradycardia\n \* History of arrhythmia requiring an implantable cardiac defibrillator\n \* Baseline prolongation of the rate-corrected QT interval (QTc; eg, repeated demonstration of QTc interval \\> 480 ms, or history of congenital long QT syndrome, or torsades de pointes)\n11. Diagnosed or treated for another malignancy within 2 years before administration of the first dose of MLN0128 or previously diagnosed with another malignancy and have any evidence of residual disease. Patients with nonmelanoma skin cancer or carcinoma in situ of any type are not excluded if they have undergone complete resection.\n\n Phase 1b Only: In addition to the previously mentioned exclusion criteria, patients meeting the following exclusion criterion are not to be enrolled in the phase 1b portion of the study:\n12. More than 3 prior chemotherapy regimens for locally advanced or metastatic disease.\n\n Phase 2 Only: In addition to the previously mentioned exclusion criteria, patients meeting the following exclusion criterion are not to be enrolled in the phase 2 portion of the study:\n13. More than 1 prior chemotherapy regimen for locally advanced or metastatic disease.",  
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"ADULT",  
"OLDER\_ADULT"  
]

Question:  
Based on the following clinical trial information, would a patient with a ERBB2 gene mutation be eligible for the clinical trial?

Answer:  
Based on the eligibility criteria provided, the clinical trial is for patients with advanced or metastatic breast cancer that is ER+ (estrogen receptor-positive) and HER2-negative (HER2-). The inclusion criteria do not specify anything regarding mutations in the ERBB2 gene, which is commonly associated with HER2 status. The critical consideration for this trial is the HER2 status, which must be negative according to the ASCO/CAP guidelines.  
  
If a patient has an ERBB2 mutation but still meets the criteria for HER2-negative status by the required testing standards, they may be eligible for the trial as long as they meet all other inclusion criteria and do not fall under any exclusion criteria. It's important to verify the HER2 status and confirm with the trial's contact or sponsor if there's any uncertainty.  
  
If the ERBB2 gene mutation indicates HER2-positive status, the patient would not be eligible for this trial, as it specifically requires HER2-negative status.