Ribociclib And Endocrine Treatment of Physician's Choice for Locoregional Recurrent, Resected Hormone Receptor Positive HER2 Negative Breast Cancer

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Eligibility Criteria to Collect Optional Correlative Blood and Tissue at Local Recurrence * Written informed consent (stage I) and HIPAA authorization for release of personal health information obtained prior to performing any study-specific procedures. NOTE: HIPAA authorization may be included in the informed consent or obtained separately. * Male or female age ≥ 18 years at the time of consent. * Patient has a histologically and/or cytologically confirmed diagnosis of estrogen-receptor positive and/or progesterone receptor positive breast cancer based on the most recently analyzed tissue sample and all tested by local laboratory. * Patient has HER2-negative breast cancer defined as a negative in situ hybridization test or an IHC status of 0, 1+ or 2+. If IHC is 2+, a negative in situ hybridization (FISH, CISH, or SISH) test is required by local laboratory testing and based on the most recently analyzed tissue sample. If there is insufficient tissue from the most recently collected sample, earlier tissue may be used on a case-by-case basis if permission is granted by the sponsor investigator. * Patient has locoregional recurrence of breast cancer: locoregional recurrence is defined as invasive recurrence in the ipsilateral breast, axilla, regional nodes, or chest wall. Inclusion Criteria for Treatment Phase: Subject must meet all of the following applicable inclusion criteria to participate in this study: * Written informed consent (stage II/ main consent) and HIPAA authorization for release of personal health information obtained prior to performing any study-specific screening procedures. NOTE: HIPAA authorization may be included in the informed consent or obtained separately. * Male or female age ≥ 18 years at the time of consent. NOTE: Both pre- and post-menopausal women are eligible. Post-menopausal status is defined as: * Prior bilateral oophorectomy * Age ≥60 * Age \<60 and amenorrhea for the last 12 or more months(in the absence of chemotherapy, tamoxifen, toremifen, or ovarian suppression) and FSH and estradiol in the postmenopausal range per local normal range. * ECOG Performance Status of 0-1 within 28 days prior to registration. * If patient is receiving tamoxifen or toremifene, a washout period of 5 half-lives (i.e. 35 days) prior to registration is required (during that period the participant can take AI). * Patient has a histologically and/or cytologically confirmed diagnosis of estrogen-receptor positive and/or progesterone receptor positive breast cancer based on the most recently analyzed tissue sample and all tested by local laboratory. * Patient has HER2-negative breast cancer defined as a negative in situ hybridization test or an IHC status of 0, 1+ or 2+. If IHC is 2+, a negative in situ hybridization (FISH, CISH, or SISH) test is required by local laboratory testing and based on the most recently analyzed tissue sample. If there is insufficient tissue from the most recently collected sample, earlier tissue may be used on a case-by-case basis if permission is granted by the sponsor investigator. * Patients have had adequate local treatment for locoregional recurrence (LRR) of breast cancer. * Locoregional recurrence is defined as recurrence in the ipsilateral breast, axilla, regional lymph nodes, or chest wall. * Local treatment is defined as either surgery, radiation therapy, or a combination of both if indicated. * Adequate local therapy is surgery with negative microscopic margins. Radiation therapy is mandated for patients with microscopically involved margins and recommended for all patients who had not received radiotherapy as part of their primary treatment. * Patients who have distant metastatic disease will not be eligible. * Prior treatment with neoadjuvant and adjuvant chemotherapy and ET is allowed. * Patients must enroll within 6 months of the last local treatment, either local surgery or radiation; or systemic chemotherapy (if patient is receiving chemotherapy), whichever occurred last. Chemotherapy after local therapy is allowed. ET for recurrent disease is allowed for up to 12 months prior to enrollment. * Patient has no contraindication to the adjuvant ET in the trial and is planned to be treated or continue treatment with ET. * Demonstrate adequate organ function as defined below; all screening labs to be obtained within 28 days prior to registration. * Hematological * Absolute Neutrophil Count (ANC): ≥ 1.5 x 109/L * Platelets: ≥ 100 x 109/L * Hemoglobin (Hgb): ≥ 9.0 g/dL * Renal ---Estimated glomerular filtration rate (eGFR): ≥ 30 mL/min/1.73m2 according to the Modification of Diet in Renal Disease (MDRD) formula * Hepatic * Bilirubin: ≤ upper limit of normal (ULN) except for patients with Gilbert's syndrome who may only be included if the total bilirubin is ≤ 3.0 × ULN or direct bilirubin ≤ 1.5 × ULN * Aspartate aminotransferase (AST): ≤ 2.5 × ULN except for patients with liver metastasis, who are only included if the AST is \< 5 × ULN * Alanine aminotransferase (ALT): ≤ 2.5 × ULN except for patients with liver metastasis, who are only included if the ALT is \< 5 × ULN * Coagulation ---International Normalized Ratio (INR) : ≤ 1.5 × ULN (unless is receiving anticoagulants and the INR is within the therapeutic range of intended use for that anticoagulant within 7 days prior to the first dose of study drug) * Electrolytes --- Potassium, Magnesium, and Total Calcium (corrected for serum albumin): Within normal limits or corrected to within normal limits with supplements. * Standard 12-lead ECG values defined as * QTcF interval at screening \< 450 msec (QT interval using Fridericia's correction) * Resting heart rate 50-90 bpm (determined from the ECG) * Females of childbearing potential who are sexually active with a male able to father a child must have a negative pregnancy test (serum or urine) within 14 days prior to registration and must be willing to use a highly effective method of contraception that does not contain estrogen and/or progesterone. See the protocol for definition of childbearing potential. * As determined by the enrolling physician or protocol designee, ability of the subject to understand and comply with study procedures for the entire length of the study. * Ability to swallow and retain oral medication. Exclusion Criteria for Treatment Phase: Subjects meeting any of the criteria below may not participate in the study: * Patient with a known hypersensitivity to any of the excipients of ribociclib. * Patient who has received prior CDK4/6 inhibitor for recurrent disease. Patients who received a CDK4/6 inhibitor in the adjuvant setting may participate if they have been off therapy for at least 1 year prior to diagnosis of recurrent disease. * Patient has had major surgery within 14 days prior to starting study drug or has not recovered from major side effects. * Pregnant or breastfeeding or planning to become pregnant during the trial (NOTE: breast milk cannot be stored for future use while the mother is being treated on study). * Patients with a prior or concurrent malignancy whose natural history or treatment has the potential to interfere with the safety or efficacy assessment of the investigational regimen are not eligible for this trial. * Patients with distant metastases of breast cancer beyond regional lymph nodes as defined by AJCC (8th edition). * Treatment with any investigational drug within 30 days prior to registration or participation in any other type of medical research judged not to be scientifically or medically compatible with this study. Enrollment or planned enrollment in another study that does not involve an investigational drug will be allowed at the discretion of the treating investigator. * Patient has impairment of gastrointestinal (GI) function or GI disease that may significantly alter the absorption of the study drugs (e.g., uncontrolled ulcerative diseases, uncontrolled nausea, vomiting, diarrhea, malabsorption syndrome, or small bowel resection). * Patient has any other concurrent severe and/or uncontrolled medical condition that would, in the investigator's judgment, cause unacceptable safety risks, contraindicate patient participation in the clinical study or compromise compliance with the protocol: (e.g., chronic pancreatitis, chronic active hepatitis, HIV, active untreated or uncontrolled fungal, bacterial or viral infections, etc.). Testing to be done at investigator's discretion. * Clinically significant, uncontrolled heart disease and/or cardiac repolarization abnormality, including any of the following: * History of documented myocardial infarction (MI), angina pectoris, symptomatic pericarditis, or coronary artery bypass graft (CABG) within 6 months prior to study entry * Documented cardiomyopathy * History of Left Ventricular Ejection Fraction (LVEF) \< 50% * Long QT syndrome or family history of idiopathic sudden death or congenital long QT syndrome, or any of the following: * Risk factors for Torsades de Pointe (TdP) including uncorrected hypocalcemia, hypokalemia or hypomagnesemia, history of cardiac failure, or history of clinically significant/symptomatic bradycardia * Concomitant medication(s) with a known risk to prolong the QT interval and/or known to cause Torsades de Pointe that cannot be discontinued or replaced by safe alternative medication (e.g., within 5 half-lives or 7 days prior to starting study drug) * Inability to determine the QTcF interval * Clinically significant cardiac arrhythmias (e.g., ventricular tachycardia), complete left bundle branch block, high-grade AV block (e.g., bifascicular block, Mobitz type II and third-degree AV block) * Systolic Blood Pressure (SBP) \>160 or \<90 mmHg * Patient is currently receiving any of the following substances and cannot be discontinued 7 days prior to Cycle 1 Day 1: * Concomitant medications, herbal supplements, and/or fruits (e.g., grapefruit, pummelos, star fruit, Seville oranges) and their juices that are strong inducers or inhibitors of CYP3A4/5, * Medications that have a narrow therapeutic window and are predominantly metabolized through CYP3A4/5. * Patient is currently receiving or has received systemic corticosteroids ≤ 2 weeks prior to starting study drug, or who have not fully recovered from side effects of such treatment. Note: The following uses of corticosteroids are permitted: a short duration (\<5 days) of systemic corticosteroids; any duration of topical applications (e.g. for rash), inhaled sprays (e.g., for obstructive airways diseases), eye drops or local injections (e.g., intra-articular). * Patient with an uncontrolled psychiatric condition that,

in the investigator's judgment, may cause unacceptable safety risks, impede research integrity and compliance, or interfere with the objectives of the study.

Conditions & Interventions

Interventions:
DRUG: Ribociclib, DRUG: Fulvestrant, DRUG: Anastrozole, DRUG: Letrozole, DRUG: Exemestane
Conditions:
Locoregional Recurrence, Hormone Receptor-positive Breast Cancer, HER2-negative Breast Cancer

More Information

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