

Testing Whether Hormone Therapy With Ribociclib is as Effective as Chemotherapy Followed by Hormone Therapy With Ribociclib for the Treatment of High Anatomic Stage Breast Cancer With Low Recurrence Risk, The RxFINE-Low Trial

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* STEP 0: Patient must be ≥ 18 years of age * STEP 0: Patient must have an Eastern Cooperative Oncology Group (ECOG) performance status of 0-2 within 28 days prior to Step 0 pre-registration * STEP 0: Patient must be a postmenopausal woman or a man * NOTE: Menopause can be determined by any of the following: * Prior bilateral oophorectomy * Age ≥ 60 years * Age < 60 years with amenorrhea for ≥ 12 months and estradiol and follicle stimulating hormone (FSH) levels in the postmenopausal range * NOTE: FSH and estradiol levels should be repeated as clinically indicated to ensure menopausal status in patients with breast cancer with chemotherapy-induced amenorrhea * STEP 0: Patient must meet one of the following staging criteria postoperatively according to American Joint Committee on Cancer (AJCC) 8th edition criteria * pT0-T3 with 3 positive ipsilateral lymph nodes (micro-or macrometastatic disease) and no planned axillary lymph node dissection after definitive surgery in the breast and axilla with curative intent. * pT0-T3 with N2 or N3 * pT3 with N0-N3 * NOTES: * Patients with T4 breast cancer are not eligible. * Positive isolated tumor cells (ITCs) in axillary nodes without micro- or macrometastasis are considered N0 for eligibility purposes. * ITC does not contribute to nodal count for staging purposes * STEP 0: Patient must have a primary breast tumor that is estrogen receptor (ER) positive with $> 10\%$ ER expression by immunohistochemistry (IHC) as per 2020 American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) Estrogen Receptor Testing Guideline. * NOTE: ER 1-10% are reported as ER low positive. These tumors have less endocrine-sensitive disease and are not eligible) * STEP 0: Patient must have a primary breast tumor that is HER2-negative by current ASCO/CAP guidelines utilizing immunohistochemistry and/or fluorescence in situ hybridization (FISH) * STEP 0: Patient may have multicentric or multifocal breast cancer if the highest stage tumor meets eligibility criteria outlined above, and the tumor sites are felt to represent a single disease process by local pathology or other sites of disease are also ER-positive ($> 10\%$) and HER2 negative, if such testing is completed. If local pathology feels that multicentric or multifocal disease may represent distinct disease processes repeat disease receptor testing is required other sites of disease must also be also ER-positive ($> 10\%$) and HER2-negative * STEP 0: For patients who have undergone a lumpectomy, the margins of the resected specimen or re-excision must be histologically free of invasive tumor and ductal carcinoma in situ (DCIS) as determined by the local pathologist. If pathologic examination demonstrates tumor at the line of resection, additional excisions may be performed to obtain clear margins. Positive posterior margin is allowed if surgeon deems no further resection possible. Patients with margins positive for lobular carcinoma in situ (LCIS) are eligible without additional resection * STEP 0: For patients who have undergone mastectomy, the margins must be free of residual gross tumor. Patients with microscopic positive margins are eligible if post-mastectomy radiation treatment (RT) of the chest wall will be administered * STEP 0: Patient must have undergone axillary staging with sentinel lymph node biopsy (SLNB), targeted axillary dissection (TAD), or axillary lymph node dissection (ALND) * STEP 0: Patient must have no evidence of locoregional or distant metastatic disease by clinical history and physical exam. Treating physician can consider additional imaging evaluation per National Comprehensive Cancer Network (NCCN) guidelines and/or institutional practice * STEP 0: Patient must be able to have Oncotype DX testing performed. * If Oncotype DX testing was previously performed, the results of Recurrence Score (RS) must be available and must meet Step 1 eligibility criteria. * If Oncotype DX testing was not performed yet, tissue from the core, excisional biopsy or surgical specimen of the tumor lesion must be available and must be shipped to Exact Sciences for determination of the Oncotype DX Recurrence Score (RS) for eligibility and stratification. * NOTE: Exact Sciences will notify the submitting institution of Recurrence Score results within two (2) weeks of receipt of the tumor specimen. Institutions will receive an email notification of eligibility status once Recurrence Score results are entered into Rave by the submitting institution * STEP 0: Patient must have had their final cancer surgery for breast cancer (including re-excision of margins) less than 16 weeks prior to Step 0 Pre-Registration. * NOTE: This excludes additional surgery for reconstructive purposes * STEP 0: Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial * STEP 0: Patients with synchronous DCIS or LCIS are eligible * STEP 0: Patient with prior history of ER-negative DCIS diagnosed at least 5 years prior to Step 0 Pre-Registration without evidence of recurrence are eligible * STEP 0: Patient must not have a prior history of invasive ER-positive breast cancer. Patients with a history of ER-negative breast cancer are eligible if they were diagnosed at least 5 years prior to Step 0 Pre-Registration and have had no evidence of recurrence * STEP 0: Patients must not have received prior endocrine therapy such as tamoxifen, raloxifene, or aromatase inhibitors for chemoprevention within 5 years prior to Step 0 Pre-Registration with the exception of a short course of endocrine therapy of less than 6 weeks duration prior to Step 0 Pre-Registration. * NOTE: The Oncotype DX for study eligibility must be performed on specimen obtained prior to initiation of any endocrine therapy * STEP 0: Patient must not be concurrently using systemic hormone replacement therapy (HRT). If receiving HRT at the time of breast cancer diagnosis, this must be discontinued prior to Step 0 Pre-Registration with appropriate washout * STEP 0: Absolute neutrophil count (ANC) $\geq 1,500/\mu\text{L}$ (obtained ≤ 28 days prior to Step 0 Pre-Registration) * STEP 0: Hemoglobin ≥ 9.0 g/dL (obtained ≤ 28 days prior to Step 0 Pre-Registration) * STEP 0: Platelets $\geq 100,000/\mu\text{L}$ (obtained ≤ 28 days prior to Step 0 Pre-Registration) * STEP 0: Total bilirubin $\leq$ institutional upper limit of normal (ULN) or $< 1.5 \times$ ULN for patients who have a bilirubin elevation in patients with well documented Gilbert's disease or similar syndrome involving slow conjugation of bilirubin (obtained ≤ 28 days prior to Step 0 Pre-Registration) * STEP 0: Aspartate aminotransferase (AST) (serum glutamic oxaloacetic transaminase [SGOT]) and alanine aminotransferase (ALT) (serum glutamic pyruvic transaminase [SGPT]) $\leq 2.5 \times$ institutional ULN (obtained ≤ 28 days prior to Step 0 Pre-Registration) * STEP 0: Estimated glomerular filtration rate (eGFR) ≥ 30 mL/minute/ 1.73 m^2 (obtained ≤ 28 days prior to Step 0 Pre-Registration) * STEP 0: Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months of Step 0 Pre-Registration are eligible for this trial * STEP 0: For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated * STEP 0: Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load * STEP 0: Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification. To be eligible for this trial, patients should be class 2 or better * STEP 0: Patient must have a standard 12-lead electrocardiogram (ECG) within 28 days prior to Step 0 Pre-Registration, documenting: * QT interval using Fridericia's correction (QTcF) < 450 msec. * Resting heart rate 50-90 beats per minute (determined from the ECG) * STEP 0: Patient must have the ability to understand and the willingness to sign a written informed consent document. Patients with impaired decision-making capacity (IDMC) who have a legally authorized representative (LAR) or caregiver and/or family member available will also be considered eligible * STEP 0: Patient must not have comorbidities considered a safety risk for standard adjuvant chemotherapy, endocrine therapy or CDK4/6 inhibitor as per Investigator's discretion * STEP 0: Patient must not have a contraindication to adjuvant chemotherapy based on treating physician's discretion * STEP 0: Patient must not have received prior chemotherapy for this malignancy * STEP 0: Patient must not have received prior CDK4/6 inhibitor * STEP 0: Patient must not have a known contraindication to ribociclib per current Food and Drug Administration (FDA) indication * STEP 0: Patient must not have a known hypersensitivity to any of the excipients of ribociclib and/or endocrine therapy (ET) (e.g. rare hereditary problems of galactose intolerance, the Lapp lactase deficiency, glucose-galactose malabsorption, and soy allergy) * STEP 0: Males must not expect to father children and males and their partners must be willing to use highly effective methods of contraception while on protocol treatment. Males must not donate sperm while on protocol treatment and for at least 12 weeks following the last dose of protocol treatment. Highly effective methods include the following: * Intrauterine device * Bilateral tubal occlusion * Vasectomized partner * Sexual abstinence If the highly effective contraceptive methods

Methods include the following: Intrauterine device, Bilateral tubal occlusion, Vasectomized partner, Coital abstinence. If the highly effective contraceptive methods are contraindicated or strictly declined by the patient, or in the event of sexual activity of low frequency, a combination of male condom with cap, diaphragm, or sponge with spermicide (double-barrier methods) is also considered an acceptable birth control method. Local regulation/guidelines are to be followed with regard to highly effective birth control method, if more restrictive * STEP 1: Patient must meet all Step 0 Pre-Registration eligibility criteria at the time of their Step 1 randomization * STEP 1: Patient must not have had any major surgery or radiotherapy within 14 days prior to Step 1 randomization * STEP 1: Patient must have a Recurrence Score (RS) of 0-25 from Oncotype DX testing from diagnostic biopsy or surgical specimen as reported by the Exact Sciences assay

Conditions & Interventions

Interventions:

DRUG: Anastrozole, PROCEDURE: Biospecimen Collection, PROCEDURE: Bone Scan, DRUG: Chemotherapy, PROCEDURE: Computed Tomography, DRUG: Exemestane, DRUG: Letrozole, PROCEDURE: Oncotype DX Breast Cancer Assay, PROCEDURE: Positron Emission Tomography, DRUG: Ribociclib Succinate

Conditions:

Anatomic Stage II Breast Cancer AJCC v8, Anatomic Stage IIIA Breast Cancer AJCC v8, Anatomic Stage IIIC Breast Cancer AJCC v8, Estrogen Receptor-Positive Breast Carcinoma, HER2-Negative Breast Carcinoma

More Information

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Principal Investigator:

IRB

Number:

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