ForPatients
by Roche

Breast CancerBreast Cancer Er-PositiveBreast Cancer HER-2 Negative

A Study of GDC-9545 Alone or in Combination With Palbociclib and/or Luteinizing Hormone-Releasing Hormone (LHRH) Agonist in Locally Advanced or Metastatic Estrogen Receptor-Positive Breast Cancer

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	5 Countries	NCT03332797 2017-002083-41 GO39932

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A Phase Ia/Ib, Multicenter, Open-Label, Dose Escalation, Dose Expansion Study Evaluating the Safety, Pharmacokinetics, and Activity of GDC-9545 Alone or in Combination With Palbociclib and/or LHRH Agonist in Patients With Locally Advanced or Metastatic Estrogen Receptor-Positive Breast Cancer

Trial Summary:

This study will evaluate the safety, pharmacokinetic (PK), pharmacodynamic (PD) activity, and preliminary anti-tumor activity of GDC-9545 as a single agent and in combination with palbociclib and/or luteinizing hormone-releasing hormone (LHRH) agonist in participants with advanced or metastatic estrogen receptor (ER)-positive (human epidermal growth factor receptor 2 [HER2]-negative) breast cancer.

Genentech, Inc.
Sponsor

Phase 1
Phase

NCT03332797 2017-002083-41 GO39932
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
Female	# 18 Years	No

Inclusion Criteria:

Inclusion Criteria for Dose Escalation:

- Histologically or cytologically proven diagnosis of adenocarcinoma of the breast with evidence of either locally recurrent disease not amenable to resection or radiation therapy with curative intent or with metastatic disease
- Estrogen receptor (ER)-positive tumor
- Human epidermal growth factor receptor 2 (HER2)-negative breast cancer as per local laboratory testing
- Measurable disease, or evaluable bone disease; that is, bone lesions that are lytic or mixed (lytic + sclerotic) in the absence of measurable lesion
- Required paired pre- and on-treatment tumor biopsies for participants with metastases that are safely accessible as determined by the investigator
- Advanced or metastatic ER-positive/HER2-negative breast cancer that has recurred or progressed while being treated with adjuvant endocrine therapy for a duration of at least 24 months and/or endocrine therapy in the incurable, locally advanced, or metastatic setting and derived a clinical benefit from therapy (i.e., tumor response or stable disease for at least 6 months)
- No more than 2 prior lines of treatment for advanced or metastatic breast cancer
- Greater than or equal to (#)2 weeks must have elapsed from the use of any other endocrine, targeted therapy or chemotherapy
- Single-Agent Cohorts (only applies to Dose Escalation): Advanced or metastatic disease that is either refractory to or intolerant of existing standard therapy or for which no effective standard therapy that confers clinical benefit is available
- Cohort B0: No prior treatment with cyclin-dependent kinase 4/6 (CDK4/6) inhibitor
- For participants undergoing 18F-fluoroestradiol-positron emission tomography (FES-PET) imaging additional restrictions on prior therapy include: #2 months must have elapsed from the use of tamoxifen; #6 months must have elapsed from the use of fulvestrant
- Postmenopausal status
- Eastern Cooperative Oncology Group (ECOG) Performance Status less than or equal to (#)1
- Resolution of all acute toxic effects of prior therapy or surgical procedures to baseline or Grade #1 (except alopecia or other toxicities not considered to be a safety risk for the patient)
- Life expectancy of #12 weeks
- Adequate organ function

Inclusion Criteria for Dose Expansion:

Same criteria as above for Dose Escalation, except for those that only apply to Dose Escalation, plus the following:

- Required paired pre- and on-treatment tumor biopsies for participants in Cohorts A1-A5, B1, and B2 with metastases that are safely accessible as determined by the investigator
- In South Korea: Must have received exactly 2 prior lines of treatment for advanced or metastatic breast cancer
- In the rest of the world: No more than 1 prior line of treatment for advanced or metastatic breast cancer (not applicable to Cohort X)

Plus the following criteria:

- Cohorts B1 and B2: No prior treatment with CDK4/6 inhibitor
- Cohorts A1, A3, A5, B1, C1, and C2 only: Postmenopausal status
- Cohorts A2, A4, and B2 only: Participants not defined as postmenopausal; Age less than (<)56 years who have medical menopause on LHRH agonist (on stable dose #4 weeks)
- No prior treatment with an oral selective estrogen receptor degrader (SERD)

- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use non-hormonal contraceptive methods with a failure rate of <1% per year during the treatment period and for 10 days after the last dose of GDC-9545 and 21 days after the last dose of palbociclib, and agreement to refrain from donating eggs during this same period
- Cohort X only: Participants enrolled on Studies GO29656 or GO29642 and received clinical benefit from GDC-0927 or GDC-0810
- Hematology, chemistry, and urinalysis collected 72 hours before Cycle 1, Day 1 deemed acceptable for dosing by the investigator
- No other endocrine therapy, targeted therapy, or chemotherapy after last dose of GDC-0927 or GDC-0810

Exclusion Criteria:

Exclusion Criteria for Dose Escalation:

- Known brain metastases that are untreated, symptomatic, or require therapy to control symptoms
- Current treatment with any systemic anti-cancer therapies for advanced disease (not applicable to Cohort X participants currently receiving GDC-0810 or GDC-0927)
- Concurrent treatment with warfarin or phenytoin
- Diagnosis of any secondary malignancy within 3 years prior to enrollment, except for appropriately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, or Stage I uterine cancer
- Active inflammatory bowel disease, chronic diarrhea, short bowel syndrome, or major upper gastrointestinal (GI) surgery including gastric resection
- Known human immunodeficiency virus (HIV) infection
- Known clinically significant history of liver disease consistent with Child-Pugh Class B or C, including active viral or other hepatitis (e.g., hepatitis B or hepatitis C virus), current alcohol abuse, or cirrhosis
- Major surgery within 4 weeks prior to enrollment
- Radiation therapy within 2 weeks prior to enrollment
- Other severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the patient inappropriate for entry into this study
- Inability or unwillingness to swallow tablets or capsules (only applies to Dose Escalation)
- Any serious medical condition or abnormality in clinical laboratory tests that, in the investigator's judgment, precludes the patient's safe participation in and completion of the study (only applies to Dose Escalation)
- History or presence of an abnormal electrocardiogram (ECG) that is clinically significant in the investigator's opinion, including complete left bundle branch block, second- or third-degree heart block, or evidence of prior myocardial infarction
- QT interval corrected using Fridericia's formula (QTcF) greater than (>)470 milliseconds (ms) demonstrated by at least two ECGs >30 minutes apart
- History of ventricular dysrhythmias or risk factors for ventricular dysrhythmias such as structural heart disease coronary heart disease clinically significant electrolyte abnormalities or family history of sudden unexplained death or long QT syndrome
- Current treatment with medications that are well known to prolong the QT interval

Exclusion Criteria for Dose Expansion:

Same criteria as above for Dose Escalation, except for those that only apply to Dose Escalation, plus the following criteria:

- Pregnant, lactating, or breastfeeding
- Additional exclusion criteria for Cohort B (Phase 1b cohort): History of venous thromboembolic event requiring therapeutic anticoagulation
- Additional exclusion criteria for Cohorts C1 and C2 only: Current treatment with medications that are well known to decrease heart rate, including beta blockers