ForPatients
by Roche

Breast CancerInoperable Breast CancerBreast Cancer Er-PositiveLocally Advanced or Metastatic Breast Cancer

A study to compare Giredestrant + Abemaciclib, Giredestrant + Ipatasertib, Giredestrant + Inavolisib, Giredestrant + Ribociclib, and Giredestrant + Everolimus with Giredestrant Monotherapy in people with inoperable, locally advanced or metastatic, estrogen receptor (ER)-positive breast cancer who had disease progression during or following treatment with a cyclin-dependent kinase 4/6 inhibitor (CDK4/6i) in the first- or second-line setting.

A Study Evaluating the Efficacy and Safety of Multiple Treatment Combinations in Participants With Breast Cancer

Trial Status	Trial Runs In	Trial Identifier
Recruiting	6 Countries	NCT04802759 2020-004889-19 CO42867

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 Ib/II, Open-Label, Multicenter, Randomized Umbrella Study Evaluating the Efficacy and Safety of Multiple Treatment Combinations in Patients With Breast Cancer (MORPHEUS- BREAST CANCER)

Trial Summary:

This is a Phase Ib/II, open-label, multicenter, randomized umbrella study in participants with breast cancer. Cohort 1 will focus on participants with inoperable, locally advanced or metastatic, estrogen receptor (ER)-positive, HER2-negative breast cancer who had disease progression during or following treatment with a cyclin-dependent kinase 4/6 inhibitor (CDK4/6i; e.g., palbociclib, ribociclib, abemaciclib) in the first- or second-line setting. Cohort 2 will focus on inoperable, locally advanced or metastatic, ER-positive, HER2-positive breast cancer with previous progression to standard-of-care anti-HER2 therapies, of which one was a trastuzumab-and-taxane-based systemic therapy (including in the early setting if recurrence occurred within 6 months of finishing adjuvant therapy) and one was a HER2-targeting antibody-drug conjugate (ADC; e.g., ado-trastuzumab emtansine or trastuzumab-deruxtecan) or a HER2-targeting tyrosine kinase inhibitor (TKI; e.g., tucatinib, lapatinib, pyrotinib or neratinib). The study is designed with the flexibility to open new treatment arms as new treatments become available, close existing treatment

arms that demonstrate minimal clinical activity or unacceptable toxicity, or modify the patient population. During Stage 1, participants in each cohort will be randomly assigned to treatment arms. Participants in the control or experimental arms who experience unacceptable toxicity, disease progression as determined by the investigator according to RECIST v1.1, or loss of clinical benefit as determined by the investigator during Stage 1 will be given the option of receiving a different treatment combination during Stage 2, provided they meet eligibility criteria and a treatment arm is open for enrollment. No Stage 2 treatment is currently available.

Hoffmann-La Roche
Sponsor

Phase 1/Phase 2
Phase

NCT04802759 2020-004889-19 CO42867
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
Female	**#18 Years**	**No**

How does the Morpheus Breast Cancer clinical trial work?

This clinical trial is recruiting people who have a type of disease called breast cancer. In order to take part, patients must have inoperable, locally advanced or metastatic, estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer.

The purpose of this clinical trial is to compare the effects, good or bad, of abemaciclib, ipatasertib, inavolisib, ribociclib or everolimus plus giredestrant versus giredestrant alone on patients with ER+, HER2- breast cancer. In this clinical trial, you will get either abemaciclib, ipatasertib, inavolisib, ribociclib or everolimus plus giredestrant or giredestrant alone.

The study is designed with the flexibility to open new treatment arms, as new treatments become available, close existing treatment arms that demonstrate minimal clinical activity or unacceptable toxicity, or modify the patient population.

How do I take part in this clinical trial?

To be able to take part in this clinical trial, you must have,

- Performance Status of 0 or 1as defined by Eastern Cooperative Oncology Group (ECOG)
- Documented estrogen receptor-positive (ER+) tumor

- Patients for whom endocrine therapy is recommended and treatment with cytotoxic chemotherapy is not indicated at time of entry into the study, as per national or local treatment guidelines
- Radiologic/objective evidence of recurrence or progression after the most recent systemic therapy for breast cancer
- Disease progression during or after first- or second-line hormonal therapy for locally advanced or metastatic disease (note: at least one line of therapy must have contained a CDK4/6i administered for a minimum of 8 weeks prior to disease progression.)
- Postmenopausal status for women
- Life expectancy #3 months
- Availability of a representative tumor specimen that is suitable for evaluation of Ki67, and/or additional biomarkers via central testing
- Prior fulvestrant therapy is allowed
- Measurable disease
- Adequate hematologic and end-organ function
- For patients receiving therapeutic anticoagulation: stable anticoagulant regimen

You must not have,

- Known HER2-positive breast cancer
- Prior treatment with cytotoxic chemotherapy for metastatic breast cancer
- Concurrent hormone replacement therapy
- Prior treatment with any of the protocol-specified study treatments
- Treatment with investigational therapy within 28 days prior to initiation of study treatment
- Systemic treatment for ER+ breast cancer within 2 weeks of Cycle 1, Day 1 or 5 half-lives of the drug prior to Cycle 1, Day 1
- Adverse events from prior anti-cancer therapy that have not resolved to Grade #1 or better, with the exception of alopecia of any grade and Grade #2 peripheral neuropathy
- Prior allogeneic stem cell or solid organ transplantation
- Major surgical procedure other than for diagnosis within 4 weeks prior to initiation of study treatment or anticipation of need for a major surgical procedure during the course of the study
- History of malignancy other than breast cancer within 2 years prior to screening, with the exception of those with a negligible risk of metastasis or death
- Uncontrolled pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures
- Uncontrolled tumor-related pain
- Uncontrolled or symptomatic hypercalcemia
- Symptomatic, untreated, or actively progressing central nervous system (CNS) metastases
- History of leptomeningeal disease
- Active tuberculosis

- Severe infection within 4 weeks prior to initiation of study treatment
- Treatment with therapeutic oral or IV antibiotics within 2 weeks prior to initiation of study treatment
- History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography scan
- Active cardiac disease or history of cardiac dysfunction
- Positive HIV test at screening or at any time prior to screening
- Active Hepatitis B or Hepatitis C virus infection
- Active inflammatory bowel disease, chronic diarrhea, short bowel syndrome, or major upper gastrointestinal (GI) surgery, including gastric resection, potentially affecting enteral absorption
- Known allergy or hypersensitivity to any of the study drugs or any of their excipients

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor. If your doctor thinks that you might be able to take part in this clinical trial, he/she may refer you to the closest clinical trial doctor. They will give you all the information you need to make your decision about taking part in the clinical trial. You can also find the clinical trial locations on this page. You will have some further tests to make sure you will be able to take the treatments given in this clinical trial. Some of these tests or procedures may be part of your regular medical care. They may be done even if you do not take part in the clinical trial. If you have had some of the tests recently, they may not need to be done again. Before starting the clinical trial, you will be told about any risks and benefits of taking part in the trial. You will also be told what other treatments are available so that you may decide if you still want to take part. While taking part in the clinical trial, both men and women (if you are not currently pregnant but can become pregnant) will need to either not have heterosexual intercourse or take contraceptive medication for safety reasons.

What treatment will I be given if I join this clinical trial?

Giredestrant, given as a pill once a day for each 28 day cycle, alone or in combination with any one of the following drugs:

- Abemaciclib, given as a pill twice a day for each 28 day cycle, or
- Ipatasertib, given as a pill once a day on days 1-21 for each 28 day cycle, or
- Inavolisib, given as a pill once a day for each 28 day cycle, or
- Ribociclib, given as a pill once a day on days 1-21 for each 28 day cycle, or
- Everolimus, given as a pill once a day for each 28 day cycle

Each group may open and close for recruitment at different times. Your chances of being placed in any group depends on how many groups are open at a given time, with no more than 35 in 100 chance of being placed in the control group.

How often will I be seen in follow-up appointments, and for how long?

You will be given the clinical trial treatment for as long as it can help you. You are free to stop this treatment at any time. After being given treatment, you will still be seen regularly by the clinical trial doctor every 28 days. Occasionally, clinic visits may occur more frequently. These hospital visits will include checks to see how you are responding to the treatment and any side effects that you may be having.

What happens if I am unable to take part in this clinical trial?

If this clinical trial is not suitable for you, you will not be able to take part. Your doctor may suggest other clinical trials that you may be able to take part in or other treatments that you can be given. You will not lose access to any of your regular care.

For more information about this clinical trial see the **For Expert** tab on the specific ForPatient page or follow this link to ClinicalTrials.gov https://clinicaltrials.gov/ct2/show/NCT04802759

Trial-identifier: NCT04802759

Inclusion Criteria:

Inclusion Criteria for Cohort 1 (Stage 1 [and Stage 2, only where indicated]):

- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1
- Documented estrogen receptor-positive (ER+) tumor
- Patients for whom endocrine therapy is recommended and treatment with cytotoxic chemotherapy is not indicated at time of entry into the study, as per national or local treatment guidelines
- Radiologic/objective evidence of recurrence or progression after the most recent systemic therapy for breast cancer
- Disease progression during or after first- or second-line hormonal therapy for locally advanced or metastatic disease (note: at least one line of therapy must have contained a CDK4/6i administered for a minimum of 8 weeks prior to disease progression.)
- Postmenopausal status for women
- Life expectancy #3 months
- Availability of a representative tumor specimen that is suitable for biomarker evaluation via central testing
- Prior fulvestrant therapy is allowed
- Stages 1 and 2: Measurable disease (at least one target lesion) according to RECIST v1.1
- Stages 1 and 2: Adequate hematologic and end-organ function
- Stages 1 and 2: Stable anticoagulant regimen for patients receiving therapeutic anticoagulation

Inclusion Criteria for Cohort 2 (Stage 1 [and Stage 2, only where indicated]):

- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1
- Histologically or cytologically confirmed and documented adenocarcinoma of the breast with metastatic or locally advanced disease not amenable to curative resection
- ER-positive, HER2-positive breast cancer
- Postmenopausal status for women
- Life expectancy #3 months

- Willingness to have a representative tumor specimen that is suitable for biomarker evaluation via central testing submitted, if available
- Prior endocrine therapy in the advanced setting allowed, including fulvestrant if given more than 28 days prior to randomization, but excluding other selective estrogen receptor degraders (SERDs)
- Stages 1 and 2: Measurable disease (at least one target lesion) according to RECIST v1.1
- Stages 1 and 2: Baseline left ventricular ejection fraction (LVEF) #50% as measured by ECHO or MUGA scans
- Stages 1 and 2: Adequate hematologic and end-organ function
- Stages 1 and 2: Stable anticoagulant regimen for patients receiving therapeutic anticoagulation

Inclusion Criteria for Cohorts 1 and 2 (Stage 2):

- Ability to initiate Stage 2 treatment within 3 months after experiencing unacceptable toxicity, disease progression as determined by the investigator according to RECIST v1.1, or loss of clinical benefit as determined by the investigator, provided that a Stage 2 slot is available and patient meets eligibility criteria for Stage 2
- Availability of a tumor specimen from a biopsy performed upon discontinuation of Stage 1 because of unacceptable toxicity to drugs, disease progression as determined by the investigator according to RECIST v1.1, or loss of clinical benefit as determined by the investigator

Exclusion Criteria:

General Exclusion Criteria for all Treatment Arms in Stage 1, Cohorts 1 and 2 (unless only applicable to one cohort, as indicated):

- Prior treatment with any of the protocol-specified study treatments
- Treatment with investigational therapy within 28 days prior to initiation of study treatment
- Systemic treatment for breast cancer within 2 weeks of Cycle 1, Day 1 or 5 half-lives of the drug prior to Cycle 1, Day 1
- Treatment with strong CYP3A4 inhibitors or inducers within 14 days or 5 drug elimination half-lives (whichever is longer) prior to randomization
- Adverse events from prior anti-cancer therapy that have not resolved to Grade #1 or better, with the exception of alopecia of any grade and Grade #2 peripheral neuropathy
- Eligible only for the control arm
- Prior allogeneic stem cell or solid organ transplantation
- Major surgical procedure other than for diagnosis within 4 weeks prior to initiation of study treatment or anticipation of need for a major surgical procedure during the course of the study
- History of malignancy other than breast cancer within 2 years prior to screening, with the exception of those with a negligible risk of metastasis or death
- Uncontrolled pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures
- Uncontrolled tumor-related pain
- Uncontrolled or symptomatic hypercalcemia
- Symptomatic, untreated, or actively progressing central nervous system (CNS) metastases
- History of leptomeningeal disease
- Active tuberculosis
- Severe infection within 4 weeks prior to initiation of study treatment
- Treatment with therapeutic oral or IV antibiotics within 2 weeks prior to initiation of study treatment
- History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography scan
- Active cardiac disease or history of cardiac dysfunction
- Positive HIV test at screening or at any time prior to screening
- Active Hepatitis B or Hepatitis C virus infection

- Active inflammatory bowel disease, chronic diarrhea, short bowel syndrome, or major upper gastrointestinal (GI) surgery, including gastric resection, potentially affecting enteral absorption
- Known allergy or hypersensitivity to any of the study drugs or any of their excipients applicable to one cohort, as indicated):
- Cohort 1 only: Known HER2-positive breast cancer
- Cohort 1 only: Concurrent hormone replacement therapy
- Cohort 1 only: Prior treatment with cytotoxic chemotherapy for metastatic breast cancer (with the exception of single agent capecitabine, which will count as a single line of therapy)
- Cohort 2 only: Dyspnea at rest due to complications of advanced malignancy, or other disease requiring continuous oxygen therapy
- Cohort 2 only: Current chronic daily treatment (continuous for >3 months) with corticosteroids (dose of 10 mg/day methylprednisolone equivalent), excluding inhaled steroids

Additional Exclusion Criteria for Giredestrant + Abemaciclib Arm and Giredestrant + Abemaciclib + Atezolizumab Arm (Cohort 1, Stage 1):

- Interstitial lung disease or severe dyspnea at rest or requiring oxygen therapy
- History of major surgical resection involving the stomach or small bowel, or a preexisting chronic condition resulting in baseline Grade 2 or higher diarrhea
- History of syncope of cardiovascular etiology, ventricular arrhythmia, or sudden cardiac arrest

Additional Exclusion Criteria for Giredestrant + Ipatasertib Arm (Cohort 1, Stage 1):

- Prior treatment with an Akt inhibitor
- Inability to swallow medication or malabsorption condition that would alter the absorption of orally administered medications
- Grade #2 uncontrolled or untreated hypercholesterolemia or hypertriglyceremia
- History of Type 1 or Type 2 diabetes mellitus requiring insulin
- History or presence of an abnormal electrocardiogram (ECG) that is clinically significant in the investigator's opinion

Additional Exclusion Criteria for Giredestrant + Inavolisib Arm (Cohort 1, Stage 1):

- Prior treatment with any PI3K, Akt, or mTOR inhibitor, or any agent whose mechanism of action is to inhibit the PI3K/Akt/mTOR pathway
- Type 2 diabetes requiring ongoing systemic treatment at the time of study entry; or any history of Type 1 diabetes
- Fasting glucose #126 mg/dL or #7.0 mmol/L and HbA1c #5.7%
- Any concurrent ocular or intraocular condition that, in the opinion of the investigator, would require medical or surgical intervention during the study period to prevent or treat vision loss that might result from that condition
- Active inflammatory or infectious conditions in either eye or history of idiopathic or autoimmune-associated uveitis in either eye
- Symptomatic active lung disease, including pneumonitis
- Inability to confirm biomarker eligibility based on valid results from either central testing of blood or local testing of blood or tumor tissue that documents one of the protocol-defined PIK3CA mutations

Additional Exclusion Criteria for Giredestrant + Ribociclib Arm (Cohort 1, Stage 1):

- Currently receiving or has received systemic corticosteroids #2 weeks prior to starting trial treatment
- Impairment of GI function or GI disease that may significantly alter the absorption of the oral trial treatments

Additional Exclusion Criteria for Giredestrant + Samuraciclib Arm (Cohort 1, Stage 1):

- Prior treatment with mTOR inhibitor
- Receipt of systemic corticosteroids (at a dose >10 mg prednisone/day or equivalent) within 14 days before the first dose of samuraciclib
- Active bleeding diatheses
- History of hemolytic anemia or marrow aplasia
- Receipt of a live-virus vaccination within 28 days or less of planned treatment start

Additional Exclusion Criteria for Giredestrant + Atezolizumab-Containing Arms (Cohort 1, Stage 1):

- Active or history of autoimmune disease or immune deficiency
- Significant cardiovascular disease (such as New York Heart Association Class II or greater cardiac disease, myocardial infarction, or cerebrovascular accident) within 3 months prior to initiation of study treatment, unstable arrhythmia, or unstable angina
- Treatment with a live, attenuated vaccine within 4 weeks prior to initiation of study treatment, or anticipation of need for such a vaccine during atezolizumab treatment or within 5 months after the final dose of atezolizumab
- Treatment with systemic immunostimulatory agents within 4 weeks or 5 drug-elimination half-lives (whichever is longer) prior to initiation of study treatment
- Treatment with systemic immunosuppressive medication within 2 weeks prior to initiation of study treatment, or anticipation of need for systemic immunosuppressive medication during study treatment
- History of severe allergic anaphylactic reactions to chimeric or humanized antibodies or fusion proteins
- Known hypersensitivity to Chinese hamster ovary cell products or recombinant human antibodies
- Prior treatment with CD137 agonists or immune checkpoint blockade therapies, including anti-CTLA-4, anti-PD-1, and anti-PD-L1 therapeutic antibodies
- Pregnant or breastfeeding, or intending to become pregnant during study treatment or within 5 months for atezolizumab

Additional Exclusion Criteria for Giredestrant + PH FDC SC + Abemaciclib Arm (Cohort 2, Stage 1):

- Interstitial lung disease or severe dyspnea
- History of major surgical resection involving the stomach or small bowel, preexisting chronic condition resulting in baseline Grade 2 or higher diarrhea, or a condition that may significantly alter the absorption of the oral trial treatments
- History of syncope of cardiovascular etiology, ventricular arrhythmia, or sudden cardiac arrest

Additional Exclusion Criteria for Giredestrant + PH FDC SC + Palbociclib Arm (Cohort 2, Stage 1):

- History of major surgical resection involving the stomach or small bowel, preexisting chronic condition resulting in baseline Grade 2 or higher diarrhea, or a condition that may significantly alter the absorption of the oral trial treatments
- Interstitial lung disease or severe dyspnea