ForPatients
by Roche

Breast Cancer HER-2 NegativeEstrogen Receptor (ER)-Positive

A clinical study to compare giredestrant with fulvestrant, both combined with a targeted therapy (CDK4/6 inhibitor) in people with ER-positive, HER2-negative breast cancer that has come back after adjuvant hormone therapy

A Study to Evaluate Efficacy and Safety of Giredestrant Compared With Fulvestrant (Plus a CDK4/6 Inhibitor), in Participants With ER-Positive, HER2-Negative Advanced Breast Cancer Resistant to Adjuvant Endocrine Therapy (pionERA Breast Cancer)

Trial Status	Trial Runs In	Trial Identifier
Recruiting	37 Countries	NCT06065748 2022-502980-39-00 CO44657

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 III randomized, open-label study evaluating efficacy and safety of giredestrant compared with fulvestrant, both combined with a CDK4/6 inhibitor, in patients with estrogen receptor-positive, HER2-negative advanced breast cancer with resistance to prior adjuvant endocrine therapy

Trial Summary:

This is a Phase III, randomized, open-label multicenter study that will evaluate the efficacy and safety of giredestrant compared with fulvestrant, both in combination with the investigator's choice of a CDK4/6 inhibitor (palbociclib, ribociclib or abemaciclib), in participants with estrogen receptor-positive (ER+), human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer who have developed resistance to adjuvant endocrine therapy.

Hoffmann-La Roche	Phase 3
Sponsor	Phase

NCT06065748 2022-502980-39-00 CO44657
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers

© 2022 F. Hoffmann-La Roche Ltd

ForPatients
by Roche

All	#18 Years	No

1. Why is the pionERA BC clinical study needed?

The body naturally produces oestrogen, a hormone which stimulates breast cancer cells that have the oestrogen receptor (known as ‘ER-positive breast cancer’) to grow. Standard treatment for ER-positive breast cancer that has not grown beyond the breast (known as ‘early’ breast cancer) includes surgery, chemotherapy and/or radiotherapy, followed by hormone therapy – known as ‘adjuvant therapy’.

In some people, adjuvant therapy can stop working (known as ‘treatment resistance’) due to changes (mutations) in the ER, and ER-positive breast cancer can come back (known as a ‘relapse’). The standard approved treatments for people who have cancer that relapses during or shortly after adjuvant treatment is a type of medicine called a ‘cyclin-dependent kinase 4 or 6 inhibitor’ (CDK4/6i) such as palbociclib, ribociclib or abemaciclib, given as a pill to be swallowed, plus the ER blocker fulvestrant, which is given as regular injections. There is a need for better hormonal therapies that can be given as a pill.

A new ER blocker called giredestrant is given as a pill and may work better than fulvestrant, particularly against tumours with mutated ERs. Giredestrant is an investigational drug, which means health authorities have not approved it for treating ER-positive breast cancer.

This study aims to compare the effects, good or bad, of giredestrant versus fulvestrant (both given with a CDK4/6i) in people with ER-positive, HER2-negative breast cancer that is resistant to prior adjuvant hormone therapy.

2. How does the pionERA BC study work?

This study is recruiting people with ER-positive, HER2-negative breast cancer that is resistant to a previous adjuvant hormone therapy. People can take part if their cancer has or has not got mutated ERs, and has grown (advanced) or spread to other parts of the body (metastatic).

People who take part in this study (participants) will be given the study treatment giredestrant or fulvestrant, both combined with a CDK4/6i (palbociclib, ribociclib or abemaciclib) until their cancer gets worse or they have unacceptable side effects. The study doctor will see them regularly. These hospital visits will include checks to see how the participants respond to the treatment, including any side effects they may have. Total time of participation in the study is expected to be, on average, about 3–5 years, depending on how well treatment works. Participants can stop study treatment and leave the study at any time.

3. What are the main results measured in the pionERA BC study?

© 2022 F. Hoffmann-La Roche Ltd

The main results measured to assess if the drug has worked (the main study endpoint) is the amount of time between the start of the study treatment and the progression of a participants' disease (progression-free survival).

The other key results include:

- How long participants live (overall survival)
- The number of participants whose tumours shrink with study treatment (overall response rate) and the amount of time this lasts if cancer worsens (duration of response)
- The number of participants whose tumours shrink or stay the same for at least 6 months with study treatment (clinical benefit rate)
- The amount of time between the start of the study treatment and:
    - participants needing chemotherapy (time to chemotherapy)
    - participants' pain, quality of life and/or ability to perform daily activities getting considerably worse (time to confirmed deterioration)
- The number and seriousness of side effects (safety and tolerability)

4. Who can take part in this study?

People can take part in this study if they have advanced or metastatic ER-positive, HER2-negative breast cancer that relapsed during or up to 1 year after adjuvant hormone therapy and are about to start their first treatment for advanced breast cancer.

People may not be able to take part in this study if they have previously received certain anti-cancer treatments, have certain other medical conditions such as heart or liver disease or certain infections, are pregnant or breastfeeding, or are intending to have a baby.

5. What treatment will participants be given in this study?

Everyone who joins this study will be split into 2 groups randomly (like flipping a coin) and given either **giredestrant** as a pill once a day OR **fulvestrant** as an injection twice during the first month and then every 4 weeks. All participants will also receive a CDK4/6i treatment as a pill (palbociclib or ribociclib once a day on Days 1#21, or abemaciclib twice a day on Days 1–28 of each 28-day cycle). Participants will have an equal chance of being placed in either group. Women who have not completed menopause and men will also be given an 'LHRH-agonist therapy' to lower their natural levels of oestrogen, which is a standard-of-care treatment. This is an open-label study, which means everyone involved, including the participant and the study doctor, will know the study treatment the participant has been given.

6. Are there any risks or benefits in taking part in this study?

© 2022 F. Hoffmann-La Roche Ltd

The safety or effectiveness of the study treatment or use may not be fully known at the time of the study. Most studies involve some risks to the participant. However, it may not be greater than the risks related to routine medical care or the natural progression of the health condition. People who would like to participate will be told about any risks and benefits of taking part in the study, as well as any additional procedures, tests, or assessments they will be asked to undergo. All of these will be described in an informed consent document (a document that provides people with the information they need to decide to volunteer for the study).

Risks associated with the clinical study drugs

Participants may have side effects (an unwanted effect of a drug or medical treatment) from the drugs used in this study. Side effects can be mild to severe, even life-threatening, and vary from person to person. Participants will be closely monitored during the study; safety assessments will be performed regularly. Participants will be told about the known side effects of **giredestrant**, **fulvestrant**, **palbociclib**, **ribociclib** and **abemaciclib** and possible side effects based on human and laboratory studies or knowledge of similar drugs. **Giredestrant**, **palbociclib**, **ribociclib** and **abemaciclib** will be given as an oral pill (by mouth); **fulvestrant** will be given by intramuscular injection (involves inserting a needle into the muscle of the buttocks). Participants will be told about any known side effects of taking pills and intramuscular injections.

Potential benefits associated with the study

Participants' health may or may not improve from participation in the clinical study. Still, the information collected may help other people with similar medical conditions in the future.

Inclusion Criteria:

- Locally advanced or metastatic adenocarcinoma of the breast, not amenable to treatment with curative intent
- Documented estrogen receptor-positive (ER+), HER2-negative (HER2-) tumor assessed locally on the most recent tumor biopsy (or an archived tumor sample if a recent tumor sample is not available for testing)
- Confirmed ESR1 mutation status (ESR1m versus ESR1nmd) in baseline circulating tumor DNA (ctDNA) through central laboratory testing
- Resistance to prior adjuvant endocrine therapy (ET), which is defined as having relapsed with prior standard adjuvant ET, on-treatment after >/=12 months or off-treatment within 12 months of completion. Prior use of adjuvant CDK4/6i is allowed (if relapse occurred >/=12 months since completion).
- No prior systemic anti-cancer therapy for advanced disease
- Measurable disease as defined per RECIST v.1.1 or non-measurable (including bone-only) disease
- Eastern Cooperative Oncology Group Performance Status (ECOG PS) 0-1
- For pre/perimenopausal women and for men: willing to undergo and maintain treatment with approved LHRH agonist therapy (as per local guidelines) for the duration of study treatment

© 2022 F. Hoffmann-La Roche Ltd

Exclusion Criteria:

- Prior systemic therapy (e.g., prior chemotherapy, immunotherapy, or biologic therapy) for locally advanced unresectable or metastatic breast cancer
- Prior treatment with another SERD (e.g., fulvestrant, oral SERDs) or novel ER-targeting agents
- Advanced, symptomatic, visceral spread that is at risk of life-threatening complications in the short term
- Active cardiac disease or history of cardiac dysfunction
- Clinically significant history of liver disease

© 2022 F. Hoffmann-La Roche Ltd