ForPatients
by Roche

Breast Cancer HER-2 Negative Estrogen 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 source of the below information is the publicly available website ClinicalTrials.gov. It has been summarised and edited into simpler language.

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 Sponsor	**Phase 3** Phase

NCT06065748 2022-502980-39-00 CO44657
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
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

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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?

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:

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- 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?

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

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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.

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