ForPatients
by Roche

Breast Cancer

A study to compare inavolisib with a non-active medicine (placebo) when combined with standard treatment in people with PIK3CA-mutated, hormone-receptor positive, HER2-negative advanced breast cancer

A Study Evaluating the Efficacy and Safety of Inavolisib Plus CDK4/6 Inhibitor and Letrozole vs Placebo + CDK4/6i and Letrozole in Participants With Endocrine-Sensitive PIK3CA-Mutated, Hormone Receptor-Positive, HER2-Negative Advanced Breast Cancer

Trial Status	Trial Runs In	Trial Identifier
Recruiting	15 Countries	NCT06790693 2024-516162-11-00 WO45654

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, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy and Safety of Inavolisib Plus a CDK4/6 Inhibitor and Letrozole Versus Placebo Plus a CDK4/6 Inhibitor and Letrozole in Patients With Endocrine-Sensitive PIK3CA-Mutated, Hormone Receptor-Positive, HER2-Negative Advanced Breast Cancer

Trial Summary:

This study will evaluate the efficacy and safety of the combination of inavolisib plus a cyclin-dependent kinase 4 and 6 inhibitor (CDK4/6i) and letrozole versus placebo plus a CDK4/6i and letrozole in the first-line setting in participants with endocrine-sensitive PIK3CA-mutated hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-), advanced breast cancer (ABC).

Hoffmann-La Roche Sponsor	**Phase 3** Phase

NCT06790693 2024-516162-11-00 WO45654
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers

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All	#18 Years	No

1. Why is this study needed?

Hormone receptor-positive (HR+) and human epidermal growth factor receptor 2-negative (HER2-) breast cancer is a type of cancer that starts in the breast. It is made up of cells that have extra hormone receptors but not extra HER2. These cells can grow more quickly than healthy cells in response to the hormones oestrogen and progesterone. Advanced cancer is often a large tumour. It may have started spreading in the body. It usually affects surrounding tissues or lymph nodes first.

Standard treatment for people with HR+ and HER2- advanced breast cancer can include medicines called CDK4/6 inhibitors (such as palbociclib) and letrozole. Some people have breast cancer that also has a change (mutation) in a small section of DNA called a gene, so that the gene is different from what is found in healthy cells. Better treatments are needed for people with HR+, HER2- breast cancer that has a mutated *PIK3CA* gene.

This study is testing a medicine called inavolisib, combined with standard treatment. The combination is being developed to treat *PIK3CA*-mutated, HR+, HER2- breast cancer.

Inavolisib with palbociclib and letrozole is an experimental combination of medicines. This means health authorities (like the U.S. Food and Drug Administration [FDA] and European Medicines Agency) have not approved this combination for the treatment of breast cancer. Inavolisib is approved by the FDA for treating *PIK3CA*-mutated, HR+, HER2- breast cancer when combined with palbociclib and another medicine called fulvestrant.

This study aims to compare the effects of inavolisib against placebo (a medicine that contains no active ingredients but looks the same and is taken in the same way as the study medicine) when combined with the standard treatment, CDK4/6 inhibitor and letrozole. This is in people with *PIK3CA*-mutated, HR+, HER2- breast cancer.

2. Who can take part in the study?

People of at least 18 years of age with *PIK3CA*-mutated, HR+, HER2- advanced breast cancer can take part in the study if their cancer cannot be removed with surgery or treated with radiation.

People may not be able to take part in this study if they are unable to swallow tablets or capsules, have breast cancer that has spread to the brain or spinal cord and is untreated or causes symptoms, or have other certain medical conditions. People who are pregnant, or currently breastfeeding cannot take part in the study.

3. How does this study work?

People will be screened to check if they are able to participate in the study. The screening period will take place from 1 month before the start of treatment.

Treatment will be given in 4-week ‘treatment cycles’. A treatment cycle is the period of treatment and recovery time before the next set of treatment is given.

This is a ‘placebo-controlled’ study. This means that participants are put in a group that will receive a medicine or a group that will receive placebo. Comparing results from the different groups helps researchers know if any changes seen result from the study medicine or occur by chance.

Everyone who joins this study will be placed into 1 of 2 groups randomly (like flipping a coin) and given either inavolisib OR placebo as a tablet (to be swallowed) every day. Everyone will also be given letrozole as a tablet (to be swallowed) every day, and palbociclib as a tablet or capsule (to be swallowed) every day for 3 weeks of each 4-week treatment cycle. Participants will have an equal chance of being placed in either group.

This is a double-blinded study. This means that neither the participants in the study nor the team running it will know which treatment is being given until the study is over. This is done to make sure that the results of the treatment are not affected by what people expected from the received treatment. However, the study doctor can find out which group the participant is in, if the participants' safety is at risk.

During this study, the study doctor will see participants 5 times in the first month treatment is given, then every 2 weeks. They will see how well the treatment is working and any unwanted effects participants may have. Some of these checks may be done via a telephone call rather than in-person. Participants will have 3 follow-up visits at 1, 3 and 6 months after completing the study treatment, during which the study doctor will check on the participant’s wellbeing. Then, the study doctor will check the wellbeing of participants every 3 months for as long as they agree to it or until the study ends using medical records, follow-up telephone calls or visits. Total time of participation in the study could be more than 5 years. Participants have the right to stop study treatment and leave the study at any time, if they wish to do so.

4. What are the main results measured in this study?

The main result measured in the study to assess if the medicine has worked is how long participants live without their cancer getting worse.

Other key results measured in the study include:

- How long participants live
- How many participants have a reduction of their cancer after treatment, and how long this response lasts

- The number of participants whose tumours shrink or stay the same for at least 6 months with study treatment
- The time it takes for a participant to have a significant worsening in certain measures (such as pain, quality of life, or being able to do daily activities)
- The number and seriousness of unwanted effects
- Participants' ability to continue on study treatment and function with any unwanted effects

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

Taking part in the study may or may not make participants feel better. But the information collected in the study can help other people with similar health conditions in the future. It may not be fully known at the time of the study how safe and how well the study treatment works. The study involves some risks to the participant. But these risks are generally not greater than those related to routine medical care or the natural progression of the health condition. People interested in taking part will be informed about the risks and benefits, as well as any additional procedures or tests they may need to undergo. All details of the study will be described in an informed consent document. This includes information about possible effects and other options of treatment.

Risks associated with the study medicines Participants may have unwanted effects of the medicines used in this study. These unwanted effects can be mild to severe, even life-threatening, and vary from person to person. During this study, participants will have regular check-ups to see if there are any unwanted effects.

Inavolisib, letrozole and palbociclib
Participants will be told about the known unwanted effects of inavolisib, letrozole and palbociclib and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects of inavolisib and palbociclib include frequent watery stools, wanting to throw up, throwing up, and a rash. Known unwanted effects of letrozole include sweating more than usual and pain in bones and joints. The study medicine(s) may be harmful to an unborn baby. Women and men must take precautions to avoid exposing an unborn baby to the study treatment.

Inclusion Criteria:

- Women or men with histologically or cytologically confirmed carcinoma of the breast
- Documented ER-positive and/or progesterone receptor-positive tumor according to American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines
- Documented HER2-negative tumor according to ASCO/CAP guidelines
- De-novo HR+ , HER2- ABC, or, alternatively, relapsed HR+ , HER2- ABC after at least 2 years of standard neoadjuvant/adjuvant endocrine therapy without disease progression during that treatment and disease-free interval of at least 1 year since the completion of that treatment
- Participants who have bilateral breast cancers which are both HR-positive and HER2-negative
- Confirmation of biomarker eligibility
- Consent to provide fresh or archival tumor tissue specimen

- Measurable disease per Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST v1.1)
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1
- Adequate hematologic and organ function within 14 days prior to initiation of study treatment

Exclusion Criteria:

- Pregnant or breastfeeding, or intention of becoming pregnant during the study or within the time frame in which contraception is required
- Metaplastic breast cancer
- Any prior systemic therapy for locally advanced unresectable or metastatic breast cancer
- Type 2 diabetes requiring ongoing systemic treatment at the time of study entry; or any history of Type 1 diabetes
- Any history of leptomeningeal disease or carcinomatous meningitis
- Known and untreated, or active CNS metastases. Participants with a history of treated CNS metastases are eligible
- Active inflammatory or infectious conditions in either eye or history of idiopathic or autoimmune-associated uveitis in either eye
- Symptomatic active lung disease
- History of or active inflammatory bowel disease
- Any active bowel inflammation
- Prior hematopoietic stem cell or bone marrow transplantation
- Treatment with strong cytochrome P450 (CYP) 3A4 inhibitors or strong CYP3A4 inducers within 4 weeks or 5 drug-elimination half-lives, prior to initiation of study treatment