ForPatients
by Roche

Breast Cancer Er-PositiveBreast CancerHER2-Positive Breast Cancer

A study to compare standard treatment plus inavolisib or a non-active placebo in people with PIK3CA-mutated, hormone receptor-positive, HER2-negative breast cancer that has spread in the body

A Study Evaluating the Efficacy and Safety of Inavolisib + Palbociclib + Fulvestrant vs Placebo + Palbociclib + Fulvestrant in Patients With PIK3CA-Mutant, Hormone Receptor-Positive, HER2-Negative, Locally Advanced or Metastatic Breast Cancer

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	28 Countries	NCT04191499 2019-002455-42 2023-505812-39-00 WO41554

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, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy and Safety of Inavolisib Plus Palbociclib and Fulvestrant Versus Placebo Plus Palbociclib and Fulvestrant in Patients With PIK3CA-Mutant, Hormone Receptor-Positive, HER2-Negative, Locally Advanced or Metastatic Breast Cancer

Trial Summary:

This study will evaluate the efficacy, safety, and pharmacokinetics of inavolisib in combination with palbociclib and fulvestrant compared with placebo plus palbociclib and fulvestrant in participants with PIK3CA-mutant, hormone receptor (HR)-positive, HER2-negative locally advanced or metastatic breast cancer whose disease progressed during treatment or within 12 months of completing adjuvant endocrine therapy and who have not received prior systemic therapy for metastatic disease.

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Phase 2/Phase 3
Phase

NCT04191499 2019-002455-42 2023-505812-39-00 WO41554
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

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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. Breast cancer can spread to nearby tissue (known as 'locally advanced cancer') and to other parts of the body (known as 'metastatic cancer').

Standard treatment for people with HR+ and HER2- breast cancer that has spread can include medicines called CDK4/6 inhibitors (such as palbociclib) and hormone blockers (such as fulvestrant). 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. Standard treatments often do not work as well for people with breast cancer that has changes in a gene called 'PIK3CA', so better treatments are needed.

This study is testing a medicine called inavolisib, combined with standard treatment. It is being developed to treat PIK3CA-mutated, HR-positive, HER2-negative breast cancer. Since this study started, inavolisib combined with palbociclib and fulvestrant has been approved by the U.S. Food and Drug Administration for treating this type of breast cancer if it worsened during or after finishing hormone therapy.

This study aims to continue to compare how well standard treatment plus inavolisib works versus standard treatment plus non-active 'placebo' in people with PIK3CA HR+ HER2- breast cancer that has spread.

2. Who can take part in the study?

People of at least 18 years of age with PIK3CA-mutated, HR+, HER2- breast cancer that has spread can take part in the study if their cancer worsened during or within 1 year of finishing a previous hormone therapy. People may not be able to take part in this study if they have previously had certain treatments, such as those similar to inavolisib, fulvestrant if given after breast cancer surgery, or any previous treatment for breast cancer that has spread in the body. People may also not take part if they have certain other medical conditions, such as diabetes, lung or heart disease, or certain infections. 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.

Everyone who joins this study will be placed into 1 of the 2 groups randomly (like flipping a coin) and given either:

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- Inavolisib, given as a tablet (to be swallowed) every day plus palbociclib, given as daily capsules or tablets for three weeks of each month and fulvestrant, given as an injection into a muscle once a month
  OR
- Placebo given as a tablet (to be swallowed) every day plus palbociclib, given as daily capsules or tablets for three weeks of each month and fulvestrant, given as an injection into a muscle once a month

Participants will have an equal chance of being placed in either group.

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’ (a medicine that contains no active ingredients but looks the same and is taken in the same way as the study medicine). Comparing results from the different groups helps researchers know if any changes seen result from the study medicine or occur by chance.

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 approximately weekly during the first month and then about once per month while they are receiving treatment. The study doctor will see how well the treatment is working and any unwanted effects participants may have. Participants will have a follow-up visit 1 month after completing the study treatment, then visits or telephone calls every 2 to 3 months, during which the study doctor will check on the participant’s wellbeing. Total duration of the study could be more than 5 years, depending on how well a participant responds to treatment. 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 many participants have a reduction of their cancer after treatment
- How many participants have a positive response to the 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
- How long people live

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- The time it takes for a participant to have a significant worsening in certain measures (such as pain, impact of their symptoms on daily life and their ability to function and enjoy life, or being able to do daily activities)
- The number and seriousness of unwanted effects
- How the study treatments get to different parts of the body, and how the body changes and gets rid of them

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 inavolisib, palbociclib, and fulvestrant

Participants may have unwanted effects from 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.

Participants will be told about the known unwanted effects of inavolisib, palbociclib, and fulvestrant and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects include a high level of sugar in the blood, feeling tired or weak, wanting to throw up, throwing up, and swelling or ulcers in the mouth or lips. Known unwanted effects of an injection into a muscle include soreness, redness, swelling, or rash on the skin where it has been pricked with a needle to give a treatment or draw blood samples. The study medicines 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:

- Confirmed diagnosis of HR+/HER2- breast cancer
- Metastatic or locally advanced disease not amenable to curative therapy
- Progression of disease during adjuvant endocrine treatment or within 12 months of completing adjuvant endocrine therapy with an aromatase inhibitor or tamoxifen
- Receiving LHRH agonist therapy for at least 2 weeks prior to Day 1 of Cycle 1 if pre/peri-menopausal
- Confirmation of biomarker eligibility (detection of specified mutation(s) of PIK3CA via specified test)
- Consent to provide fresh or archival tumor tissue specimen

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- Measurable disease per Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST v1.1); evaluable "bone-only" disease is not eligible; "bone-only" disease with at least one measurable, soft-tissue component, even if considered disease that is limited to bone but has lytic or mixed lytic/blastic lesions and at least one measurable soft-tissue component per RECIST v1.1 may be eligible
- Eastern Cooperative Oncology Group Performance Status of 0 or 1
- Life expectancy of > 6 months
- Adequate hematologic and organ function within 14 days prior to initiation of study treatment

Exclusion Criteria:

- Metaplastic breast cancer
- Any history of leptomeningeal disease or carcinomatous meningitis
- Any prior systemic therapy for metastatic breast cancer
- Prior treatment with fulvestrant or any selective estrogen-receptor degrader, with the exception of participants that have received fulvestrant or any selective estrogen-receptor degrader as part of neoadjuvant therapy only and with treatment duration of no longer than 6 months
- 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
- Known and untreated, or active CNS metastases. Patients with a history of treated CNS metastases may be eligible
- Active inflammatory or infectious conditions in either eye, or any eye conditions expected to require surgery during the study treatment period
- Symptomatic active lung disease, or requiring daily supplemental oxygen
- History of inflammatory bowel disease or active bowel inflammation
- Anti-cancer therapy within 2 weeks before study entry
- Investigational drug(s) within 4 weeks before randomization
- Prior radiotherapy to >= 25% of bone marrow, or hematopoietic stem cell or bone marrow transplantation
- Chronic corticosteroid therapy or immunosuppressants
- Pregnant, lactating, or breastfeeding, or intending to become pregnant during the study or within 2 weeks after the final dose of study treatment
- Major surgical procedure, or significant traumatic injury, within 28 days prior to Day 1 of Cycle 1

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