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Breast Cancer Er-PositiveMetastatic Breast CancerBreast CancerHER2-Positive Breast Cancer

A clinical trial to compare RO7198574 plus inavolisib with RO7198574 plus placebo as maintenance treatment after first treatment in people with PIK3CA#mutated HER2#positive breast cancer that has grown (locally advanced) or spread (metastatic)

A Study to Evaluate the Efficacy and Safety of Inavolisib in Combination With Phesgo Versus Placebo in Combination With Phesgo in Participants With PIK3CA-Mutated HER2-Positive Locally Advanced or Metastatic Breast Cancer

Trial Status	Trial Runs In	Trial Identifier
Recruiting	27 Countries	NCT05894239 2022-502046-28-00 WO44263

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 in Combination With Phesgo Versus Placebo in Combination With Phesgo As Maintenance Therapy After First Line Induction Therapy in Participants With PIK3CA-Mutated HER2-Positive Locally Advanced or Metastatic Breast Cancer

Trial Summary:

This study will evaluate the efficacy and safety of inavolisib in combination with Phesgo (pertuzumab, trastuzumab, and rHuPH20 injection for subcutaneous use) compared with placebo in combination with Phesgo, as maintenance therapy, after induction therapy in participants with previously untreated HER2-positive advanced breast cancer (ABC).

Hoffmann-La Roche	Phase 3
Sponsor	Phase

NCT05894239 2022-502046-28-00 WO44263
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers

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All	#18 Years	No

1. Why is the WO44263 clinical trial needed?

Standard treatment for people with HER2#positive breast cancer that has grown and cannot be removed by surgery (locally advanced) or has spread to other parts of the body (metastatic) is chemotherapy with a combination of drugs called pertuzumab and trastuzumab (PH) named induction therapy, followed by maintenance therapy with PH. A drug called RO7198574 is a version of PH given as an injection under the skin. Some people have HER2-positive breast cancer that has a change, also called a mutation, in a gene called *PIK3CA*. Breast cancers with this type of mutation can get worse more quickly, so new therapies are needed to slow cancer growth. Drugs such as inavolisib block the activity of mutated *PIK3CA* to slow the growth of cancer cells and may make PH maintenance therapy work for longer. Inavolisib is an experimental drug – health authorities have not approved it as a treatment for breast cancer. This clinical trial aims to compare the effects, good or bad, of RO7198574 plus inavolisib versus RO7198574 plus placebo as maintenance therapy for people with *PIK3CA*#mutated HER2#positive breast cancer.

2. How does the WO44263 clinical trial work?

This clinical trial is recruiting people with *PIK3CA*#mutated HER2#positive breast cancer that is locally advanced or metastatic. People who take part in this clinical trial (participants) must first be given the standard induction therapy (PH or RO7198574, plus a chemotherapy called a taxane). The clinical trial treatment RO7198574 plus inavolisib or RO7198574 plus placebo will then be given for as long as it stops cancer getting worse. The clinical trial doctor will see participants every week for the first month then once a month. These hospital visits will include checks to see how the participant responds to the treatment and any side effects they may have. Total time in the clinical trial will depend on how a participants' cancer responds to treatment and could be from 1 day to 9 years or longer. Participants can stop trial treatment and leave the clinical trial at any time and will not lose access to their regular healthcare.

3. What are the main endpoints of the WO44263 clinical trial?

The main clinical trial endpoint (the main result measured in the trial to see if the drug has worked) is the amount of time between the start of the trial and participants' cancer getting worse or the tumour getting bigger (known as 'progression-free survival').

The other clinical trial endpoints include:

- How long participants live (overall survival)
- How many participants have a reduction in their tumour size or how much their cancer has progressed (known as ‘overall response rate’)
- How much time passes between when participants’ cancer first responds to treatment and when their cancer gets worse (known as ‘duration of response’)
- The number of participants who respond to treatment or have tumours that stay the same size for at least approximately 6 months (known as ‘clinical benefit rate')
- The number and seriousness of any side effects
- Change in health-related quality of life
- How the body processes inavolisib

4. Who can take part in this clinical trial?

People can take part in this trial if they are over the age of 18 and have *PIK3CA*#mutated HER2#positive breast cancer that is locally advanced or metastatic.

People may not be able to take part in this trial if they have:

Previously received certain treatments for advanced HER2-positive breast cancer

Cancer that has spread to the brain or spinal cord and causes symptoms, and is untreated or is currently being treated with certain medicines

Certain other medical conditions such as heart, lung, liver or eye problems, diabetes, virus infections, or they are pregnant or breastfeeding or are planning to become pregnant during the trial or within 7 months after the final dose of RO7198574

5. What treatment will participants be given in this clinical trial?

After induction therapy, everyone will be given **RO7198574** as an injection under the skin every 3 weeks, and either **inavolisib** OR **placebo** as a tablet (to be swallowed) daily. Participants will have an equal chance of being placed in either group. This is a ‘placebo-controlled’ clinical trial, which means that one of the groups will be given RO7198574 along with a substance with no active ingredients (known as a ‘placebo’); it looks like the drug being tested but does not contain any real medicine. Comparing results from the different groups helps the researchers know whether any changes seen result from the drug or occur by chance. This is a double-blinded trial, which means that neither the participant nor the clinical trial doctor can choose or know the group the participant is in, until the trial is over. This approach helps to prevent bias and expectations about what will happen. However, the participant’s clinical trial doctor can find out which group the participant is in, if their safety is at risk.

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

The safety or effectiveness of the experimental treatment or use may not be fully known at the time of the trial. Most trials 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 clinical trial, 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 clinical trial).

Risks associated with the clinical trial drugs

Participants may have side effects (an unwanted effect of a drug or medical treatment) from the drugs used in this clinical trial. Side effects can be mild to severe, even life-threatening, and vary from person to person. Participants will be closely monitored during the clinical trial and safety assessments will be performed regularly. Participants will be told about the known side effects of **RO7198574** and **inavolisib**, and possible side effects based on human and laboratory studies or knowledge of similar drugs. **RO7198574** will be given as an injection under the skin (subcutaneous injection). Participants will be told about any known side effects of subcutaneous injection. **Inavolisib** or **placebo** will be given as a tablet to be swallowed. Participants will be told about any known side effects of swallowing tablets.

Potential benefits associated with the clinical trial

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

For more information about this clinical trial see the For Expert tab on the specific ForPatients page or follow this link to ClinicalTrials.gov: https://classic.clinicaltrials.gov/ct2/show/NCT05894239

Inclusion Criteria:

- Eastern Cooperative Oncology Group (ECOG) Performance Status 0 or 1
- Histologically or cytologically confirmed and documented adenocarcinoma of the breast with metastatic or locally advanced disease not amenable to curative resection
- Confirmation of HER2 biomarker eligibility based on valid results from central testing of tumor tissue documenting HER2-positivity

- Confirmation of PIK3CA-mutation biomarker eligibility based on valid results from central testing of tumor tissue documenting PIK3CA-mutated tumor status
- Disease-free interval from completion of adjuvant or neoadjuvant systemic non-hormonal treatment to recurrence of >= 6 months
- LVEF (left ventricular ejection fraction) of at least 50% measured by echocardiogram (ECHO) or multiple-gated acquisition scan (MUGA)
- Adequate hematologic and organ function prior to initiation of study treatment

Exclusion Criteria:

- Prior treatment in the locally advanced or metastatic setting with any PI3K, AKT, or mTOR inhibitor or any agent whose mechanism of action is to inhibit the PI3K-AKT-mTOR pathway
- Any prior systemic non-hormonal anti-cancer therapy for locally advanced or metastatic HER2-positive breast cancer prior to initiation of induction therapy
- History or active inflammatory bowel disease
- Disease progression within 6 months of receiving any HER2-targeted therapy
- Type 2 diabetes requiring ongoing systemic treatment at the time of study entry; or any history of Type 1 diabetes
- Participants with active HBV infection
- Clinically significant and active liver disease, including severe liver impairment, viral or other hepatitis, current alcohol abuse, or cirrhosis
- Symptomatic active lung disease, including pneumonitis or interstitial lung disease
- Any history of leptomeningeal disease or carcinomatous meningitis
- Serious infection requiring IV antibiotics within 7 days prior to Day 1 of Cycle 1
- 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