ForPatients
by Roche

Inflammatory Breast CancerLocally Advanced Breast CancerBreast Cancer HER-2 PositiveBreast CancerEarly Breast CancerHER2-Positive Breast Cancer

A Study to Evaluate Patient Preference for Home Administration of Fixed-Dose Combination of Pertuzumab and Trastuzumab for Subcutaneous Administration in Participants With Early or Locally Advanced/Inflammatory HER2-Positive Breast Cancer

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	17 Countries	NCT05415215 2023-506380-33-00 MO43110

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 IIIB, Multinational, Multicenter, Randomized, Open-Label Study to Evaluate Patient Preference for Home Administration of Fixed-Dose Combination of Pertuzumab and Trastuzumab for Subcutaneous Administration in Participants with Early or Locally Advanced/Inflammatory HER2-Positive Breast Cancer

Trial Summary:

This is a Phase IIIb, multinational, multicenter, randomized, open-label study to evaluate patient preference of the fixed-dose combination of pertuzumab and trastuzumab for subcutaneous use (PH FDC SC) administration in the home setting compared with the hospital setting during the cross-over period of adjuvant treatment in participants with early or locally advanced/inflammatory human epidermal growth factor receptor 2-positive (HER2+) breast cancer.

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

NCT05415215 2023-506380-33-00 MO43110
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is this study needed?

HER2, also known as human epidermal growth factor receptor 2, is a protein involved in normal cell growth. It can be made in larger than normal amounts by some types of cancer cells, including breast cancer, and cause cancer cells to grow more quickly. The standard treatment for HER2-positive breast cancer that has not spread in the body or has only spread to nearby tissues is a combination of medicines. These medicines are called pertuzumab and trastuzumab. They are given with chemotherapy. Previous studies show that pertuzumab and trastuzumab treatment works equally well when given as a drip into a vein (which takes a few hours), or when given as an injection under the skin (which takes a few minutes). This study will look at whether people with HER2-positive breast cancer prefer this treatment as injections under the skin at home, or in a hospital.

2. Who can take part in the study?

People (males and females) of 18 years of age or older with HER2-positive breast cancer, that has not spread in the body or has only spread to nearby tissues, can take part in the study if they plan to have surgery to remove their tumour and are able to have injections under the skin of their thigh.

People may not be able to take part in this study if they have breast cancer that has spread to other parts of the body. People who are pregnant, or currently breastfeeding cannot take part in the study.

3. How does this study work?

Participants may have to be a part of this study for about 1 and a half to 2 years. Participants will be screened to check if they are able to participate in the study. The screening period will take place from 1 day to 1 month before the start of treatment. Treatment will be given in 2 parts:

Part 1 (before surgery)

Everyone who joins this study will join 1 of 2 groups at random (like flipping a coin) and be given chemotherapy in the hospital AND either:

- **Group A:** pertuzumab and trastuzumab, given as a drip into a vein every 3 weeks
- **Group B:** OR pertuzumab and trastuzumab, given as an injection under the skin every 3 weeks

Participants will have a 1 in 3 chance of being in Group A, and a 2 in 3 chance of being in Group B. 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. Participants will then have surgery to remove the cancer within 6 weeks of their last dose of pertuzumab and trastuzumab with chemotherapy.

Part 2 (from 2 weeks after surgery)

Participants from Part 1 with remaining cancer cells in tissues removed by surgery will be given trastuzumab emtansine as a drip into a vein every 3 weeks in the hospital. They may also be given radiotherapy.

Participants from Part 1 who have no cancer remaining in tissues removed by surgery will be given pertuzumab and trastuzumab as an injection under the skin every 3 weeks for 2 treatment cycles in the hospital. They may also be given radiotherapy. This will happen during the 'run-in' period. Participants will then join 1 of 2 groups randomly (like flipping a coin) and be given pertuzumab and trastuzumab as an injection under the skin every 3 weeks during the 'cross-over' period. This will be either:

- In the hospital for 2 months, then in their home for 2 months
- OR, in their home for 2 months, then in the hospital for 2 months

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

Participants can then choose to receive pertuzumab and trastuzumab at home or in the hospital, given as an injection under the skin every 3 weeks. This is called the 'treatment continuation' period. All treatments will be given by a nurse or a doctor.

During this study, the study doctor will see participants every 3 weeks. Some visits will take place in the participant's home by a nurse. The doctor or nurse will see how well the treatment is working and any unwanted effects participants may have. Participants will have a follow-up visit after 6 to 9 months of completing study treatment, during which the study doctor will check on the participant's wellbeing. Total time of participation in the study will be about 1 and a half to 2 years. Participants have the right to stop study treatment and leave the study at any time if they wish to do so. Participants will not lose access to regular care if they stop study treatment.

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

The main result measured in the study is the number of participants who prefer treatment at home rather than in the hospital, based on the responses provided in a Patient Preference Questionnaire.

Other key results measured in the study include:

- The number of healthcare professionals who find it more convenient and faster to give treatment as an injection under the skin than as a drip into a vein
- The number of participants who have no cancer following treatment in Part 1 and surgery
- Changes in how participants' health impacts their daily life and their ability to function and enjoy life

- The number of participants who ask for treatment at home rather than in the hospital during the treatment continuation period
- The number, type and seriousness of unwanted effects that participants experience

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.

Pertuzumab, trastuzumab and trastuzumab emtansine

Participants will be told about the known unwanted effects of pertuzumab, trastuzumab and trastuzumab emtansine, and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects of pertuzumab and trastuzumab include frequent, watery stools, feeling or being sick, hair loss, feeling tired or weak, difficulty pooing, and fever. Known unwanted effects of trastuzumab emtansine include difficulty breathing, feeling tired or weak, feeling or being sick and fever.

Pertuzumab and trastuzumab will be given as a drip into a vein or an injection under the skin. Trastuzumab emtansine will be given as a drip into a vein. Known unwanted effects of drips into a vein and injections under the skin include feeling or being sick, a feeling of coldness that makes the body shiver, low or high blood pressure, fever, reddening of the skin, pain or discomfort in the head, a rapid heart rate or heart beats out of rhythm, frequent, watery stools, shortness of breath, cough and throat irritation or swelling. 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:

- Eastern Cooperative Oncology Group (ECOG) performance status 0-1
- Intact skin at planned site of subcutaneous (SC) injections
- Left ventricular ejection fraction (LVEF) greater than or equal to (#)55% by echocardiogram (ECHO) or multiple-gated acquisition scan (MUGA)
- Negative human immunodeficiency virus (HIV) test at screening
- Negative hepatitis B surface antigen (HBsAg) test at screening
- Positive hepatitis B surface antibody (HBsAb) test at screening, or negative HBsAb at screening accompanied by either of the following: Negative total hepatitis B core antibody (HBcAb); Positive total HBcAb test followed by a negative (per local laboratory definition) hepatitis B virus (HBV) DNA test
- Negative hepatitis C virus (HCV) antibody test at screening, or positive HCV antibody test followed by a negative HCV RNA test at screening
- For female participants of childbearing potential: agreement to remain abstinent or use contraception and agree to refrain from donating eggs during the treatment period and for 7 months after the final dose of the study treatment
- For male participants: agreement to remain abstinent or use a condom, and agree to refrain from donating sperm during the treatment period and for 7 months after the final dose of study treatment

Disease-specific Inclusion Criteria:

- Female and male participants with stage II-IIIC early or locally advanced/inflammatory human epidermal growth factor receptor 2-positive (HER2+) breast cancer
- Primary tumor >2 centimetres (cm) in diameter, or node-positive disease
- HER2+ breast cancer confirmed by a local laboratory prior to study enrollment. HER2+ status will be determined based on pretreatment breast biopsy material and defined as 3+ by Immunohistochemistry (IHC) and/or positive by HER2 amplification by in situ hybridization (ISH) following American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) guidelines 2018 and updates (Wolff et al. Arch Pathol Lab Med 2018)
- Hormone receptor status of the primary tumor determined by local assessment following American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) guidelines and updates (Allison et al. J Clin Oncol 2020)
- Agreement to undergo mastectomy or breast conserving surgery after neoadjuvant therapy, including the axillary nodes
- Availability of formalin-fixed, paraffin-embedded (FFPE) tumor tissue block for local confirmation of HER2 and hormone receptor status following current ASCO/CAP guidelines

Inclusion Criteria for Treatment with Adjuvant PH FDC SC:

- Completed the neoadjuvant phase of this study and underwent surgery, and achieved pathologic complete response (pCR), defined as eradication of invasive disease in the breast and axilla according to the current American Joint Committee on Cancer (AJCC) staging system classification, and using the resected specimen by the local pathologist on the basis of guidelines to be provided in a pathology manual
- Adequate wound healing after breast cancer surgery per investigator's assessment to allow initiation of study treatment within less than or equal to (#)9 weeks of last systemic neoadjuvant therapy

Exclusion Criteria:

- Stage IV (metastatic) breast cancer
- History of concurrent or previously treated non-breast malignancies, except for appropriately treated 1) non-melanoma skin cancer and/or 2) in situ carcinomas, including cervix, colon, and skin. A participant with previous invasive non-breast cancer is eligible provided he/she has been disease free for more than 5 years

- Participants who are pregnant or breastfeeding or intending to become pregnant during the study or within 7 months after the final dose of study treatments
- Treatment with investigational therapy within 28 days prior to initiation of study treatment
- Active, unresolved infections at screening requiring treatment
- Participants who may have had a recent episode of thromboembolism and are still trying to optimize the anticoagulation dose and/or have not normalized their International Normalized Ratio (INR)
- Serious cardiac illness or medical conditions
- History of ventricular dysrhythmias or risk factors for ventricular dysrhythmias
- Inadequate bone marrow function
- Impaired liver function
- Renal function with creatinine clearance <50 mL/min using the Cockroft-Gault formula and serum creatinine >1.5x upper limit of normal (ULN)
- Major surgical procedure unrelated to breast cancer within 28 days prior to study entry or anticipation of the need for major surgery during the course of study treatment
- Current severe, uncontrolled systemic disease that may interfere with planned treatment
- Any serious medical condition or abnormality in clinical laboratory tests that precludes an individual's safe participation in and completion of the study
- Treatment with a live vaccine (e.g., FluMist) in the 30 days prior to initiation of study treatment, or anticipation of need for such a vaccine during treatment or within 90 days after the final dose of study treatment
- Known active liver disease, for example, active viral hepatitis infection, autoimmune hepatic disorders, or sclerosing cholangitis
- Known hypersensitivity to any of the study drugs, excipients, and/or murine proteins or a history of severe allergic or immunological reactions, e.g., difficult to control asthma
- Current chronic daily treatment with corticosteroids
- Assessment by the investigator as being unable or unwilling to comply with the requirements of the protocol

Cancer-specific Exclusion Criteria for Neoadjuvant Phase:

- Participants who have received any previous systemic therapy for treatment or prevention of breast cancer, or previous chest irradiation for the treatment of cancer
- Participants who have a past history of ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS) if they have received any systemic therapy for its treatment or radiation therapy to the ipsi- or contralateral breast cancer
- Participants with high-risk for breast cancer who have received chemopreventive drugs in the past
- Participants with multicentric breast cancer, unless all tumors are HER2+
- Participants with bilateral breast cancer
- Participants who have undergone an excisional biopsy of primary tumor and/or axillary lymph nodes
- Axillary lymph node dissection (ALND) prior to initiation of neoadjuvant therapy
- Sentinel lymph node biopsy (SLNB) prior to neoadjuvant therapy

Exclusion Criterion for Treatment with Adjuvant Trastuzumab Emtansine (Arm E):

- Current Grade #3 peripheral neuropathy (according to the NCI CTCAE v5.0)