A PHASE III, RANDOMIZED, OPEN-LABEL STUDY EVALUATING THE EFFICACY AND SAFETY OF GIREDESTRANT IN COMBINATION WITH PHESGO VERSUS PHESGO AFTER INDUCTION THERAPY WITH PHESGO TAXANE IN PATIENTS WITH PREVIOUSLY UNTREATED HER2-POSITIVE, ESTROGEN RECEPTOR-POSITIVE LOCALLY-ADVANCED OR METASTATIC BREAST CANCER

14/08/2025 08:36:17

Main Information

Primary registry identifying number
LBCTR2024015502

Protocol number
WO43571

MOH registration number

Study registered at the country of origin
No

Study registered at the country of origin: Specify
The Study is not registered in the IMP country of origin Switzerland, however it is being conducted in several countries worldwide including EU countries sample of HAs Approval are attached. Please advise if any other documents needed from our side

Type of registration
Prospective

Type of registration: Justify
N/A

Date of registration in national regulatory agency

Primary sponsor
F. Hoffmann-La Roche Ltd

Primary sponsor: Country of origin
Switzerland

Date of registration in primary registry
19/06/2025

Date of registration in national regulatory agency

Public title
A PHASE III, RANDOMIZED, OPEN-LABEL STUDY EVALUATING THE EFFICACY AND SAFETY OF GIREDESTRANT IN COMBINATION WITH PHESGO VERSUS PHESGO AFTER INDUCTION THERAPY WITH PHESGO TAXANE IN PATIENTS WITH PREVIOUSLY UNTREATED HER2-POSITIVE, ESTROGEN RECEPTOR-POSITIVE LOCALLY-ADVANCED OR METASTATIC BREAST CANCER

Acronym
heredERA

Scientific title
A PHASE III, RANDOMIZED, OPEN-LABEL STUDY EVALUATING THE EFFICACY AND SAFETY OF GIREDESTRANT IN COMBINATION WITH PHESGO VERSUS PHESGO AFTER INDUCTION THERAPY WITH PHESGO TAXANE IN PATIENTS WITH PREVIOUSLY UNTREATED HER2-POSITIVE, ESTROGEN RECEPTOR-POSITIVE LOCALLY-ADVANCED OR METASTATIC BREAST CANCER

Acronym
heredERA

Brief summary of the study: English

This Phase III, randomized, two-arm, open-label, multicenter study will evaluate the efficacy and safety of Phesgo plus giredestrant compared with Phesgo after induction with Phesgo + taxane in participants with HER2-positive, ER-positive advanced breast cancer (metastatic or locally advanced disease not amenable to curative treatment) who have not previously received a systemic non-hormonal anti-cancer therapy in the advanced setting.
Study treatment is comprised of two phases: induction therapy followed by study maintenance therapy. Approximately 812 participants will be enrolled into the induction therapy phase, and approximately 730 participants will be randomized in the maintenance therapy phase.
Participants who are still in the induction therapy phase after this target is reached will be also be allowed to enter the maintenance therapy phase, if they are deemed eligible by the investigator

Brief summary of the study: Arabic

هذه الدراسة من المرحلة الثالثة، عشوائية، ثنائية مجموعة، مفتوحة، متعددة المراكز ستقيم الفعالية سلامة فيزجوفي توليفة جيريدسترانت بالمقارنة مع فيزجو بعد العلاج الحثي باستخدام فيزجو+ تاكسان في المشاركون المصابون بسرطان الثدي المتقدم الأيجابي لمستقبالت اللاأستروجين أو (المرض النقيلي أو المتقدم موضعيا غير القابل للعلاج الشفائي) الذين لم يتلقوا من قبل علاجا جهازيا مضادا للسرطان غير HER2إيجابي هرموني في المرحلة المتقدمة.
، مشاركا في مرحلة العلاج الحثي812يتكون علاج الدراسة من مرحلتين: العلاج الحثي يتبعه علاج المداومة للدراسة. سيتم إدراج ما يقرب من مشاركا عشوائيا في مرحلة علاج المداومة. كما سيسمح للمشاركين الذين لا يزالون في مرحلة العلاج الحثي بعد730وسيوضع ما يقرب من تحقيق هذا الهدف بدخول مرحلة علاج المداومة إذا اعتبرهم الباحث مؤهلين

Health conditions/problem studied: Specify

PREVIOUSLY UNTREATED HER2-POSITIVE, ESTROGEN RECEPTORPOSITIVE LOCALLY-ADVANCED OR METASTATIC BREAST CANCER

Interventions: Specify

During the induction therapy phase, participants will receive four to six cycles of Phesgo in combination with a taxane (i.e., docetaxel or paclitaxel, as per the standard of care.). At the investigator's discretion, participants who tolerate six cycles of induction therapy well and do not experience progressive disease (PD) may be given up to two additional cycles: up to a maximum of eight cycles as per the standard of care. Participants who have received one or two cycles of Phesgo (or trastuzumab SC with pertuzumab IV, or PH IV) with docetaxel or paclitaxel prior to enrollment are eligible and these additional cycles will count towards eligibility for the maintenance phase.
Following the induction therapy phase, eligible participants will be randomized into themaintenance therapy phase during which they will receive Phesgo plus giredestrant or Phesgo in 21-day cycles until disease progression, unacceptable toxicity, withdrawal of consent, death, or predefined study end, whichever occurs first.
Participants will be followed for safety for 28 days after the final dose of study treatment, including a treatment discontinuation visit at 28 days (□3 days) after the final dose of Phesgo. Thereafter, information on survival and new anti-cancer therapy will be collected every 3 months until death (unless the participant withdraws consent or the Sponsor terminates the study). The survival follow-up period for participants remaining in the study will conclude at the time of the final overall survival (OS) analysis.
A study schema is provided in Section 1.2 & Figure 1in attached protocol. Refer to Section 1.3 for a schedule of activities (Table 1) in attached protocol, schedule of PRO assessments (Table 2, Table 3, and Table 4) in attached protocol and a sample collection schedule (Table 5) in attached protocol.

Key inclusion and exclusion criteria: Inclusion criteria

●Signed Informed Consent Form
●Participants (females, regardless of menopausal status, and males) who are aged ≥18 years at the time of signing Informed Consent Form
- For women: postmenopausal or premenopausal status, defined as follows:
A participant is considered postmenopausal if any of the following definitions are met:
Prior bilateral oophorectomy
Age>60 years
Age <60 years and amenorrheic for 12 months or more in the absence of chemotherapy or ovarian suppression, and FSH and estradiol in the postmenopausal ranges
-Pre- or perimenopausal (i.e., not meeting the criteria for postmenopausal)
●Ability to comply with the study protocol, in the investigator's judgment
Histologically or cytologically confirmed and documented adenocarcinoma of the breast with metastatic or locally-advanced disease not amenable to curative resection.
-HER2-positive ABC confirmed by a central laboratory prior to study enrollment. HER2-positive status will be determined based on primary or metastatic lesion and defined as 3□ by immunohistochemistry (IHC) and/or positive by HER2 amplification by in situ hybridization (ISH) with a ratio of ≥ 2 for the number of HER2 gene copies to the number of signals for chromosome 17 copies. Participants will be eligible provided that at least one HER2 test (IHC or ISH) yields a positive result
-A representative formalin-fixed, paraffin-embedded (FFPE) tumor specimen in a paraffin block (preferred) or at least 20 slides containing unstained, freshly cut, serial sections that meet the criteria outlined in Section 8.7 must be submitted prior to study enrollment. In exceptional circumstances, 11−19 slides are acceptable provided that other eligibility requirements are met; however, a minimum of 20 slides is highly preferred. For China, the number of slides required for eligibility will be based on Human Genetics Resources Administration of China (HGRAC) specifications.

-Documented ER-positive tumor according to the American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines, assessed locally and defined as ≥ 1% of tumor cells staining positive for ER, preferentially based on the same lesion that was used to determine HER2 positivity.
●At least one measurable lesion and/or non-measurable disease evaluable according to RECIST version 1.1
-Note for participants who receive induction therapy off study: baseline tumor assessments must meet the criteria as listed in Section 8.1.1.1 in attached protocol

●Disease-free interval from completion of adjuvant or neoadjuvant systemic non-hormonal treatment to recurrence of ≥ 6 months
●Eastern Cooperative Oncology Group (ECOG) Performance Status 0 or1
●LVEF of at least 50% measured by ECHO or MUGA
●Adequate hematologic and end-organ function, defined by the following laboratory test results, obtained within 7 days prior to enrollment:
- ANC ≥1.5 x 109 /L (1500 cells/□L) with one exception:
Participants with benign ethnic neutropenia: ANC ≥1.3□109 /L (1300/□L)
– Platelet count ≥ 100,000 cells/□L
– Hemoglobin ≥9.0 g/dL
Participants may receive RBC transfusions to obtain this level
– Estimated creatinine clearance ≥ 30mL/min as calculated per institutional guidelines
– INR and aPTT ≤1.5 □ upper limit of normal (ULN) (except for participants receiving anticoagulation therapy)
For participants receiving warfarin, a stable INR between 2 and 3 is required.
For participants receiving heparin, PTT (or aPTT) between 1.5 and 2.5 ULN is required.
If anticoagulation therapy is required for a prosthetic heart valve, stable INR between 2.5 and 3.5 is permitted.
– Serum AST and ALT ≤ 3 □ ULN (for participants with documented liver metastasis: AST and ALT≤ 5 □ULN)
– Serum total bilirubin (TBILI) ≤1.5□ ULN, except for participants with Gilbert syndrome (≤ 3□ ULN), for whom direct bilirubin should be within the normal range
– Serum albumin ≥ 25 g/L (2.5 g/dL)
●For women of childbearing potential: Participants who agree to remain abstinent (refrain from heterosexual intercourse) or use contraception, and agree to refrain from donating eggs, as defined below:
Women must remain abstinent or use non-hormonal contraceptive methods with a failure rate of □ 1% per year during the treatment period and for 7 months after the final dose of Phesgo. A woman is considered to be of childbearing potential if she is postmenarchal, has not reached a postmenopausal state (≥12 continuous months of amenorrhea with no identified cause other than menopause), and is not permanently infertile due to surgery (i.e., removal of ovaries, fallopian tubes, and/or uterus) or another cause as determined by the investigator (e.g., Müllerian agenesis). The definition of childbearing potential may be adapted for alignment with local guidelines or regulations.
Examples of non-hormonal contraceptive methods with a failure rate of □ 1% per year include bilateral tubal ligation, male sterilization, and copper intrauterine devices.
The reliability of sexual abstinence should be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the individual. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or postovulation methods) and withdrawal are not adequate methods of contraception. If required per local guidelines or regulations, locally recognized adequate methods of contraception and information about the reliability of abstinence will be described in the local Informed Consent Form.

●For men: participants who agree to remain abstinent (refrain from heterosexual intercourse) or use a condom, and agree to refrain from donating sperm, as defined below:
With a female partner of childbearing potential or pregnant female partner, men must remain abstinent or use a condom during the treatment period and for 7 months after the final dose of Phesgo to avoid exposing the embryo. Men must refrain from donating sperm during this same period. The reliability of sexual abstinence should be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the individual. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or postovulation methods) and withdrawal are not adequate methods of preventing drug exposure. If required per local guidelines or regulations, information about the reliability of abstinence will be described in the local Informed Consent Form.

Maintenance Phase Criteria

Participants are eligible to be randomized into the maintenance phase of the study only if all of the following criteria apply:
●Complete a minimum of four cycles of induction therapy, defined as either
– 4 Phesgo injections □ 4 docetaxel infusions
or
– 4 Phesgo injections □ 12 paclitaxel infusions Note: If a participant has received one or two cycles of induction therapy prior to enrollment, these cycles are to be counted towards the required number of cycles for eligibility of the maintenance phase (e.g., if the participant was given one cycle of Phesgo [or trastuzumab SC with pertuzumab IV, or PH IV] □docetaxel prior to enrollment, a minimum of 3 cycles of Phesgo □ docetaxel are required prior to entering the maintenance phase)

●Achieve a minimum of SD [or Non-CR/Non-PD for participants with nonmeasureable disease] (i.e., did not experience PD) according to RECIST v1.1 at the last tumor assessment during the induction therapy phase
●LVEF of ≥50% at the last assessment during the induction therapy phase
In addition, patients should not consume grapefruit, grapefruit juice, grapefruit supplements, or Seville oranges (potent CYP3A inhibitors) within 3 days prior to initiation of giredestrant treatment in Arm B

Key inclusion and exclusion criteria: Gender

Both

Key inclusion and exclusion criteria: Specify gender

Key inclusion and exclusion criteria: Age minimum

18

Key inclusion and exclusion criteria: Age maximum

100

Key inclusion and exclusion criteria: Exclusion criteria

Potential participants are excluded from the study if any of the following criteria apply:

●Previous systemic non-hormonal anti-cancer therapy in the MBC or ABC setting
Note: Up to one line of single-agent ET given in the metastatic or locallyadvanced setting will be allowed.
One or two cycles of Phesgo (or trastuzumab SC with pertuzumab IV, or PH IV) with docetaxel or paclitaxel in the first line ABC setting is allowed prior to enrollment, provided no limiting toxicities or PD have occurred.

●Previous treatment with approved or investigative anti-HER2 agents except Phesgo (or trastuzumab SC with pertuzumab IV, or PH IV), single-agent trastuzumab IV or SC, ado-trastuzumab emtansine, lapatinib, and neratinib in the neoadjuvant or adjuvant setting
●Disease progression within 6 months of receiving trastuzumab, with or without pertuzumab (IV, SC, or fixed-dose combination), or ado-trastuzumab emtansine in the adjuvant setting
●Non-resolution of all acute toxic effects of prior anti-cancer therapy or surgical procedures to NCI CTCAE v5.0 Grade 1 or better (except alopecia, Grade ≤2 peripheral neuropathy, or other toxicities that are not considered a safety risk for the participant per investigator's judgment)
● History of persistent Grade ≥ 2 (NCI-CTC, Version 5.0) hematological toxicity resulting from previous adjuvant or neo-adjuvant therapy
● History of exposure to the following cumulative doses of anthracyclines
– Doxorubicin □360 mg/m2
– Liposomal doxorubicin □500 mg/m2
– Epirubicin □720 mg/m2
– Mitoxantrone □120 mg/m2
– Idarubicin □90 mg/m2 If another anthracycline or more than one anthracycline has been used, then the cumulative dose must not exceed the equivalent of 360 mg/m2 doxorubicin. (See Appendix 10 in protocol for dose conversions).
●Known active uncontrolled or symptomatic central nervous system (CNS) metastases, carcinomatous meningitis, or leptomeningeal disease Participants with a history of CNS metastases or cord compression are eligible if they have been definitively treated with local therapy (e.g., radiotherapy, surgery), are clinically stable, and have not been treated with anticonvulsants or corticosteroids within 2 weeks prior to enrollment.
●Dyspnea at rest due to complications of advanced malignancy, or other disease requiring continuous oxygen therapy
●Pregnant or breastfeeding, or intending to become pregnant during the study or within 7 months after the final dose of Phesgo
o Women of childbearing potential must have a negative serum pregnancy test result within 14 days prior to initiation of induction therapy
●Treated with investigational therapy within 28 days prior to initiation of induction therapy · Treated with localized palliative radiotherapy within 14 days prior to initiation of induction therapy
●Concurrent participation in any other therapeutic clinical trial
●Known hypersensitivity to any of the study medications or to excipients of recombinant human or humanized antibodies
●Current chronic daily treatment (continuous for □3 months) with corticosteroids (dose of 10 mg/day methylprednisolone or equivalent), excluding inhaled steroids
●Poorly controlled hypertension (e.g., systolic blood pressure □180 mm Hg or diastolic blood pressure □ 100 mmHg)
●Known clinically significant history of liver disease consistent with Child-Pugh Class B or C, active liver disease including active viral or other hepatitis virus (e.g., hepatitis B or hepatitis C), autoimmune hepatic disorders, or sclerosing cholangitis, current alcohol abuse, or cirrhosis Active viral infection is clinically defined as requiring treatment with antiviral therapy or the presence of positive test results for hepatitis B (hepatitis B surface antigen [HBsAg] and/or total hepatitis B core antibody [anti-HBc]) or HCV antibody. Patients are not required to have HBV, or HCV assessments at screening if these assessments have not been previously performed. Patients that have tested positive for anti-HBc would be eligible if tests for HBsAg and PCR are HBV DNA are negative. Patients who have been cured of their HCV infection (must have an undetectable viral load i.e., a sustained virologic response for 3 months after completing treatment) are eligible to enroll. Patients that have tested positive for the HCV antibody would be eligible if tests for HCV RNA are negative. If the patient is a carrier of HCV and tests positive for HCV RNA, they would not be considered eligible. For patients who have been successfully treated for viral hepatitis, the possibility of re-activation of the virus or reinfection with viral hepatitis should be considered by the Investigator and the overall potential benefits associated with study treatment for the patient should be deemed to exceed the overall risks.
●Active cardiac disease or history of cardiac dysfunction, including any of the following:
– History or presence of symptomatic bradycardia or resting heart rate □50 beats per minute (BPM) at screening Participants on stable dose of a □-blocker or calcium channel antagonist for preexisting baseline conditions (e.g., hypertension) may be eligible if heart rate is at least 50 bpm.
– History of angina pectoris or myocardial infarction within 12 months prior to study entry – History of NCI CTCAE v5.0 Grade ≥3 symptomatic congestive heart failure (CHF) or New York Heart Association (NYHA) ClassII or greater cardiomyopathy
– QT interval corrected through use of Fridericia's formula (QTcF) □470 ms, history of long or short QT syndrome, Brugada syndrome or known history of corrected QT interval prolongation, or torsades de pointes
– History or presence of an abnormal ECG that is clinically significant in the investigator's opinion, including complete left bundle branch block, second- or third-degree heart block, sick sinus syndrome, long QT syndrome, or evidence of prior myocardial infarction
– History of ventricular dysrhythmias or risk factors for ventricular dysrhythmias such as structural heart disease (e.g., severe left ventricular systolic dysfunction, left ventricular hypertrophy), coronary heart disease (symptomatic or with ischemia demonstrated by diagnostic testing), clinically significant electrolyte abnormalities (e.g., hypokalemia, hypomagnesemia, hypocalcemia), or family history of long QT syndrome
– High-risk uncontrolled arrhythmias (i.e., atrial tachycardia with a heart rate ≥100/min at rest, significant ventricular arrhythmia [ventricular tachycardia], or higher-grade atrioventricular [AV]-block, such as second degree AV-block Type 2 [Mobitz 2] or third-degree AV-block)
– Serious cardiac arrhythmia not controlled by adequate medication, severe conduction abnormality
– Clinically significant valvular heart disease
– Evidence of transmural infarction on ECG
●Major surgical procedure or significant traumatic injury within 14 days prior to enrollment or anticipation of need for major surgery during induction therapy.
Note: Should surgery be necessary during the study, participants should be allowed to recover for a minimum of 14 days prior to subsequent Phesgo treatment, regardless of the phase of the study (induction therapy or maintenance). Placement of implantable central venous access device (e.g., Port-a-Cath□) is not considered a major surgery.
●Active inflammatory bowel disease, chronic diarrhea, short bowel syndrome, or major upper gastrointestinal surgery, including gastric resection, potentially affecting enteral absorption
● Concurrent, serious, uncontrolled infections, or known infection with HIV with the following exception:

Individuals who are HIV positive are eligible provided they are stable on anti-retroviral therapy for ≥4 weeks, have a CD4 count ≥350 cells/□L, and have an undetectable viral load and no history of AIDS-defining opportunistic infections within 12 months prior to enrollment.
Proper taxane dose reduction due to PK interactions with the antiretroviral therapy must be pursued according to local prescribing information.
●Serious COVID-19 infection within 14 days prior to enrollment; however, no screening testing for SARS-CoV-2 is required
● Serious infection requiring oral or IV antibiotics within 7 days prior to screening
●Any serious medical condition or abnormality in clinical laboratory tests that precludes an individual's safe participation in the study
●History of malignancy within 5 years prior to screening, with the exception of the cancer under investigation in this study and malignancies with a negligible risk of metastasis or death (e.g., 5-year OS rate □ 90%), such as adequately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, localized prostate cancer, ductal carcinoma in situ, or Stage I uterine cancer
●For pre- and perimenopausal women: known hypersensitivity to LHRHa, unless willing to undergo bilateral oophorectomy prior to ET initiation that requires ovarian suppression (i.e., experimental arm and AI use in the control arm)
●For all men: known hypersensitivity to LHRHa
●For pre- and perimenopausal women, and men: not willing to undergo and maintain treatment with approved LHRHa therapy for the duration of ET that requires gonadal function suppression (i.e., experimental arm, and AI use in the control arm).
●Treatment with strong CYP3A4 inhibitors or inducers within 14 days or 5 drug-elimination half-lives, whichever is longer, prior to initiation of giredestrant treatment in Arm B.

Type of study

Interventional

Type of intervention

Pharmaceutical

Type of intervention: Specify type

N/A

Trial scope

Other

Trial scope: Specify scope

Study design: Allocation

Randomized controlled trial

Study design: Masking

Open (masking not used)

Study design: Control

Active

Study phase

3

Study design: Purpose

Treatment

Study design: Specify purpose

N/A

Study design: Assignment

Parallel

Study design: Specify assignment

N/A

IMP has market authorization

No

IMP has market authorization: Specify

Name of IMP

Gierdestrant

Year of authorization

Month of authorization

Type of IMP

Others

Pharmaceutical class

- Giredestrant (GDC-9545) is a potent, orally bioavailable, small-molecule, selective estrogen receptor degrader (SERD).
- Phesgo is a ready-to-use formulation containing fixed-dose combination (FDC) of pertuzumab and trastuzumab with recombinant human hyaluronidase PH20 (rHuPH20) for subcutaneous (SC) administration. The active ingredients (monoclonal antibodies: pertuzumab and trastuzumab) in PH FDC SC are identical to the active ingredients in the approved Perjeta□ (pertuzumab intravenous [IV]) and Herceptin□ (trastuzumab IV or SC) formulations. Phesgo is Date of MA: 12-04-2023 with the following license numbers:
Phesgo 1200mg/ 600 mg: 118721/1
Phesgo 600/600 mg: 118621/1

Therapeutic indication

PREVIOUSLY UNTREATED HER2-POSITIVE, ESTROGEN RECEPTORPOSITIVE LOCALLY-ADVANCED OR METASTATIC BREAST CANCER

Therapeutic benefit

Taking into account giredestrant's efficacy data in patients with ER-positive, HER2 negative BC, the safety profiles for Phesgo and giredestrant, the expected synergy of such a combination, the unmet medical need of better survival outcomes for patients with ER-positive, HER2-positive ABC, and the risk mitigation measures for the study, the benefit risk ratio is expected to be acceptable for Phesgo plus giredestrant following four to six cycles of a Phesgo taxane for patients with previously untreated, locally-advanced unresectable or metastatic ER-positive/HER2-postitive BC.

Study model

N/A

Study model: Explain model

N/A

Study model: Specify model

N/A

Time perspective

N/A

Time perspective: Explain time perspective

N/A

Time perspective: Specify perspective

N/A

Target follow-up duration

Target follow-up duration: Unit

Number of groups/cohorts

Biospecimen retention

Samples with DNA**

Biospecimen description

Locally Performed Tests - Mandatory;
- Hematology (WBC count, RBC count, hemoglobin, hematocrit, platelet count, and differential count (neutrophils, eosinophils, basophils, monocytes, lymphocytes, and other cells)
- Chemistry panel (serum): sodium, potassium, magnesium, chloride, glucose, BUN or urea, creatinine, creatine clearance (at screening only, if necessary to confirm eligibility), total protein, albumin, phosphorus, calcium, total bilirubin, ALP, ALT, AST, and LDH
- Coagulation: INR (or PT) and aPTT (or PTT)
- FSH
- Estradiol
- Urine and Blood Pregnancy test
- Urinalysis, including dipstick (pH, specific gravity, glucose, protein, ketones, and blood)
Central Lab Tests;
- Plasma and serum PK samples - Mandatory
- Plasma and serum ADA samples - Mandatory
- Blood and Plasma samples for biomarkers - Mandatory
- Blood sample for WGS/WES - Mandatory
- Blood & tissue sample for RBR - Optional
- Tissue Samples: Archival tissue sample from the primary tumor (preferred) and/or
metastatic sites must be submitted to assess HER2 status to confirm eligibility & retrospectively ER/ Status . Only participants who do not have tissue specimens that meet eligibility requirements may undergo a biopsy during the screening period - Mandatory
- Tissue Samples: Biomarkers (Tumor tissue sample) if deemed clinically feasible

Target sample size

922

Actual enrollment target size

Date of first enrollment: Type
Actual

Date of first enrollment: Date
18/07/2022

Date of study closure: Type
Actual

Date of study closure: Date
31/01/2032

Recruitment status
Recruiting

Recruitment status: Specify

Date of completion

IPD sharing statement plan
Yes

IPD sharing statement description

During this study, health and personal information ("information") about the patient will be collected. The below describes the protection, use, and sharing of the patient's information, which consists of the following:
-Information in the patient medical record, which is held by study site
-Information (including imaging data) that is collected or produced during this study ("study data"), which is held by the study site, Roche, Roche affiliates, and Roche's representatives (people and companies who work for Roche)
The patient privacy is very important, and Roche uses many safeguards to protect patients' privacy, in accordance with applicable data privacy laws and laws related to the conduct of clinical trials.
The patients study data and samples will be labeled with a participant identification (ID) number that is unique to each patient and not related to or derived from information that identifies him/her (such as his/her name, his/her picture, or any other personally identifying information).
Roche, Roche affiliates, and Roche's representatives will only have access to study data and samples labeled with a participant ID number, except when accessing the patients' medical record under certain circumstances, as described below:
The patient's information (including his/her medical record, which contains personal information that can identify the patient) may need to be reviewed to make sure the study is being done properly or to check the quality of the information. This information will be kept private. The following people and groups of people may review and/or copy this information:
- Authorized individuals (such as study monitors and auditors) representing Roche and Roche's collaborators and licensees (people and companies who partner with Roche)
- The Institutional Review Board or Ethics Committee (people responsible for protecting the rights and safety of people who take part in research studies)
- Regulatory authorities (government agencies involved in keeping research safe
for people)
Roche, Roche affiliates, and Roche's collaborators and licensees may use study data labeled with patients participant ID number.
The patients study data may also be shared with independent researchers or government agencies, but only after personal information that can identify the patients have been removed.
Patients study data may be combined with other people's data and/or linked to other data collected from study patients. The patients study data may be used to help better understand why people get diseases and how to best prevent, diagnose, and treat diseases, and to develop and provide access to new medicines, medical devices, and health care solutions. These data will not include information that identifies the patients.
The patients' information will not be given to insurance company or employer, unless required by law. If the results from this study are published in a medical journal or presented at a scientific meeting, the patients will not be identified.
Information from this study will be retained by the study site for 15 years after the end of the study or for the length of time required by applicable laws, whichever is longer. In addition, Roche will retain the study data for 25 years after the final study results have been reported or for the length of time required by applicable laws, whichever is longer.
The Patients study data may be used or shared for the purposes of this study and for research related to cancer, common pathways (links) among diseases, the use of experimental drugs in disease therapy, and/or the development of tests or tools that help with detecting or understanding cancer.
Patients study data may be used by and/or shared with Roche, Roche affiliates, Roche's collaborators and licensees, the Institutional Review Board or Ethics Committee, and regulatory authorities. The patients study data and samples may be analyzed in any country worldwide.

Additional data URL

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
EU Trial Number	2022-500014-26-00

Sources of Monetary or Material Support

Name
F. Hoffmann-La Roche Ltd

Secondary Sponsors

No Sponsors

Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Fadi Nasr	Hotel-Dieu de France	Lebanon	+961 3 622 845	nasrfadi@hotmail.com	Oncologist - HDF
Scientific	Fadi Nasr	Hotel-Dieu de France	Lebanon	+961 3 622 845	nasrfadi@hotmail.com	Oncologist - HDF
Public	Hady Ghanem	Lebanese American University Medical Center-Rizk Hospita	Lebanon	+961 76 477 647	hady.ghanem@laumcrh.com	Oncologist - LAU
Scientific	Hady Ghanem	Lebanese American University Medical Center-Rizk Hospita	Lebanon	+961 76 477 647	hady.ghanem@laumcrh.com	Oncologist - LAU
Public	Marcel Massoud	Notre Dame Des Secours	Lebanon	+961 70 502 377	marcel.massoud@gmail.com	Oncologist
Scientific	Marcel Massoud	Notre Dame Des Secours	Lebanon	+961 70 502 377	marcel.massoud@gmail.com	Oncologist
Public	Nagi El Saghir	AUB	Lebanon	00961-1-350000	ns23@aub.edu.lb	Oncologist
Scientific	Nagi El Saghir	AUB	Lebanon	00961-1-350000	ns23@aub.edu.lb	Oncologist

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Hotel-Dieu de France	Fadi Nasr	Oncologist	Approved
Lebanese American University Medical Center-Rizk Hospita	Hady Ghanem	Oncologist	Approved
Notre Dame Des Secours	Marscel Massoud	Oncologist	Approved
AUB	Nagi El Saghir	Oncologist	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
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American University of Beirut Medical Center	31/05/2024	Prof. Nagi Saghir	irb@aub.edu.ib	+961 1 35 00 00 – Ext 5445

Countries of Recruitment

Name
Oman
United Arab Emirates
United States of America
Jordan
Brazil
Russian Federation
Thailand
Taiwan
Turkey

China
Germany
United Kingdom
Mexico
Argentina
Colombia
India
Spain
France
Belgium
Italy
Portugal
Saudi Arabia
Egypt
Qatar
Kenya
Poland
Uganda
Lebanon

Health Conditions or Problems Studied

Condition	Code	Keyword
PREVIOUSLY UNTREATED HER2-POSITIVE, ESTROGEN RECEPTORPOSITIVE LOCALLY-ADVANCED OR METASTATIC BREAST CANCER	Breast (D48.6)	Breast Cancer

Interventions

Intervention	Description	Keyword
Phesgo	pertuzumab 1200 mg and trastuzumab 600 mg/15 ml	Phesgo
Phesgo	pertuzumab 600 mg and trastuzumab 600 mg/10 ml	Phesgo
Giredestrant	Giredestrant 30 mg	Giredestrant

Primary Outcomes

Name	Time Points	Measure
To evaluate the efficacy of Phesgo plus giredestrant compared with Phesgo	End of Study	PFS, defined as the time from randomization to the first occurrence of disease progression or death from any cause (whichever occurs first), as determined by the investigator according to RECIST v1.1

Key Secondary Outcomes

Name	Time Points	Measure
Secondary Objectives: To evaluate the efficacy of Phesgo plus giredestrant compared with Phesgo	End of Study	□ OS, defined as the time from randomization to death from any cause □ ORR (following randomization), defined as the proportion of participants with a CR or PR on two consecutive occasions □ 4 weeks apart, as determined by the investigator according to RECIST v1.1 □ DOR (following randomization), defined as the time from the first occurrence of a documented objective response to disease progression or death from any cause (whichever occurs first), as determined by the investigator according to RECIST v1.1 □ CBR (following randomization), defined as the proportion of participants with SD for □24 weeks or a CR or PR, as determined by the investigator according to RECIST v1.1 □ Mean and mean changes from baseline score in function (role, physical) and HRQoL by cycle and between treatment arms as assessed through the use of the Functional and GHS/QoL scales of the EORTC QLQ-C30
Secondary Objectives: To evaluate the safety of Phesgo plus giredestrant compared with Phesgo	End of Study	□ Incidence and severity of adverse events, with severity determined according to NCI CTCAE v5.0 □ Change from baseline in targeted clinical laboratory test results
Exploratory Objectives: To evaluate the efficacy of Phesgo plus giredestrant compared with Phesgo	End of Study	□ Mean and mean changes from baseline score in disease/treatment-related symptoms by cycle and between treatment arms as assessed by all symptom items/scales of the EORTC QLQ-C30 and EORTC QLQ-BR23 □ Proportion of participants reporting a clinically meaningful deterioration in pain severity, defined as a □2-point increase from baseline on the “worst pain” item score from the BPI□SF questionnaire
Exploratory Objectives: To evaluate effects of Phesgo plus giredestrant compared with Phesgo on work productivity and activity	End of Study	Changes in patient-reported WPAI scores at specified timepoints
Exploratory Objectives: To evaluate health utility of participants treated with Phesgo plus giredestrant compared with Phesgo to generate utility scores for use in economic models	End of Study	Utility scores of the EQ-5D-5L questionnaire

Exploratory Objectives: To evaluate the tolerability of Phesgo plus giredestrant compared with Phesgo from the participant's perspective	End of Study	□ Presence, frequency of occurrence, severity, and/or degree of interference with daily function of symptomatic treatment toxicities (nausea, vomiting, diarrhea, rash, joint pain, fatigue, hot flashes), as assessed through use of the NCI PRO-CTCAE □ Proportion of participants reporting each response option at each assessment timepoint by treatment arm for treatment side-effect bother single-item GP5 from the FACT□G □ Change from baseline in symptomatic treatment toxicities and treatment side-effect bother, as assessed through use of the PRO-CTCAE and the overall treatment side-effect bother item, respectively
Exploratory Objectives: To characterize the giredestrant, pertuzumab, and trastuzumab PK profile when given in combination	End of Study	□ Concentrations of pertuzumab and trastuzumab in serum at specified time points □ Plasma concentrations of giredestrant at specified time points
Exploratory Objectives: To evaluate the potential relationships between Phesgo and giredestrant exposure and the safety, efficacy, immunogenicity, or biomarker endpoints when Phesgo and giredestrant are given in combination	End of Study	□ Relationship between pertuzumab PK and efficacy, safety, immunogenicity, or biomarker endpoints □ Relationship between trastuzumab PK and efficacy, safety, immunogenicity, or biomarker endpoints □ Relationship between giredestrant PK and efficacy, safety, immunogenicity, or biomarker endpoints
Exploratory Objectives: To evaluate the immune response to pertuzumab, trastuzumab, and rHuPH20	End of Study	□ Incidence of pertuzumab ADAs during the study relative to the prevalence of ADAs at baseline □ Incidence of trastuzumab ADAs during the study relative to the prevalence of ADAs at baseline □ Incidence of rHuPH20 ADAs during the study relative to the prevalence of ADAs at baseline
Exploratory Objectives: To evaluate potential effects of ADAs when Phesgo and giresdestrant are given in combination	End of Study	□ Relationship between pertuzumab ADA status and efficacy, safety, or PK endpoints □ Relationship between trastuzumab ADA status and efficacy, safety, or PK endpoints □ Relationship between rHuPH20 ADA status and efficacy, safety, or PK endpoints
Exploratory Objectives: To identify and/or evaluate biomarkers that are predictive of response to Phesgo and giredestrant (i.e., predictive biomarkers), are early surrogates of efficacy, are associated with progression to a more severe disease state (i.e., prognostic biomarkers), are associated with acquired resistance to Phesgo and giredestrant, are associated with susceptibility to developing adverse events or can lead to improved adverse event monitoring or investigation (i.e., safety biomarkers), can provide evidence of Phesgo and giredestrant activity (i.e., pharmacodynamic biomarkers), or can increase the knowledge and understanding of disease biology and drug safety	End of Study	Relationship between biomarkers in blood, plasma and tumor tissue (listed in Section 8.7 in attached protocol) and efficacy, safety, PK, immunogenicity, or other biomarker endpoints

Trial Results

Summary results

Study results globally

Date of posting of results summaries

Date of first journal publication of results

Results URL link

Baseline characteristics

Participant flow

Adverse events

Outcome measures

URL to protocol files