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A study to evaluate the processing by the body of giredestrant in female participants of non-childbearing potential with impaired liver functions

Submission date 07/10/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 10/10/2022	**Overall study status** Completed	
Last Edited 17/11/2022	**Condition category** Other	

Plain English summary of protocol

Background and study aims
Breast cancer is a disease in which cells in the breast grow out of control. It is the most common cancer diagnosed in women, and accounts for approximately 15% of all cancer deaths. Most breast cancers grow with the help of the female hormone receptors called estrogen receptors (ER). A receptor is a part of a cell that attaches to a specific substance and this attachment causes changes, such as the release/making of a protein. Hence, treatments of breast cancer are mainly centered around therapies that modify these receptors (endocrine therapies). However, in many participants the cancer comes back after treatment (called relapse), or they experience reduction in the effectiveness of medication (resistance) over a period of time. Giredestrant is a drug being developed for the treatment of breast cancer. Health authorities have not yet approved giredestrant for the treatment of breast cancer or any other disease. The main aim of the study is to measure how much of the drug gets into the blood stream and how long it takes the body to get rid of it when given to female participants who are unable to become pregnant, with normal liver function or differing levels of liver problems (impairment). In addition, the safety and tolerability of the giredestrant and any side effects that may occur also will be evaluated.

Who can participate?
Female participants of non-childbearing potential between 18 and 75 years of age with normal liver function or differing levels of liver impairment

What does the study involve?
Participants will need to be a part of this study for about 4 weeks. The study will include the following parts:
1. A screening part of up to 28 days to check the eligibility of participants to take part in the study
2. A dosing/confinement part of up to 9-12 days depending on whether the participants have normal or impaired liver function where participants will receive single dose of giredestrant by

mouth on Day 1 after an overnight fast of at least 8 hours. Participants will be required to fast for at least 4 hours after taking giredestrant.
3. A follow-up part during which participants will receive a follow-up telephone call 28 (±2) days following drug administration.

What are the possible benefits and risks of participating?
Participant's health may or may not improve in this study, but the information that is learned may help other people who have breast cancer in the future. Participants will receive monetary compensation for taking part in the study.

Participants may have side effects from giredestrant, or procedures used in this study. These can be mild to severe and even life threatening, and they can vary from person to person. There may be side effects that are not known at this time. The potential side effects associated with giredestrant, and other procedures are listed below:
Risks associated with Giredestrant:
Very Common Side Effects: Pain or stiffness in joints (arthralgia), loose stools (diarrhea), tiredness (fatigue), muscle or bone pain (musculoskeletal pain), nausea, possible liver damage (abnormal liver tests)
Common Side Effects: Slow heart rate, dizziness, hot flush, vomiting, headache
Potential Side Effects: Blood clots, damage to the kidneys, changes to female reproductive organs, including fluid-filled lump in the ovary (ovarian cysts) and decreased uterine weight, female infertility; menopausal symptoms
2. Risk associated with study procedures:
Blood Sampling: Drawing blood can cause pain, bruising, or infection where the needle is inserted. Some people experience dizziness, fainting, or upset stomach when their blood is drawn
Electrocardiograms (ECG): ECG patches may cause a skin reaction such as redness or itching. Participants may also experience localized skin discomforts and/or hair loss associated with the placement of ECG leads.

There may be a risk in exposing an unborn child to study drug, and all risks are not known at this time. Participants who can become pregnant cannot take part in this study.

Where is the study run from?
F. Hoffmann-La Roche Ltd (USA)

When is the study starting and how long is it expected to run for?
June 2022 to December 2024

Who is funding the study?
F. Hoffmann-La Roche Ltd (USA)

Who is the main contact?
global-roche-genentech-trials@gene.com

Contact information

Type(s)
Scientific

Contact name

Dr Clinical Trials

Contact details
1 DNA Way
South San Francisco
United States of America
94080
+1 (0)888 662 6728
global-roche-genentech-trials@gene.com

Additional identifiers

Protocol serial number
GP44228

Study information

Scientific Title
A phase I, open-label, single-dose, parallel-cohort study to evaluate the pharmacokinetics of giredestrant in female subjects of non-childbearing potential with impaired hepatic functions

Study objectives
The aim of the study is to evaluate pharmacokinetics (PK) and safety of a single oral dose of giredestrant in female participants of non-childbearing potential with mild, moderate, and severe hepatic impairment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 24/082022, Salus IRB (2111 W. Braker Lane, Suite 100, Austin, Texas 78758, USA; +1 512-380-1244; salus@salusirb.com), ref: none provided

Primary study design
Interventional

Study design
Open-label multicenter parallel-cohort single-dose phase I study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Pharmacokinetics of giredestrant in females with impaired hepatic functions

Interventions
Giredestrant 30 milligrams (mg): Participants with normal hepatic function and mild, moderate and severe hepatic impairment will receive a single dose of giredestrant, 30 mg, orally on Day 1, after a fast of 8 hours. Participants will be required to fast for up to 4 hours postdose.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Giredestrant

Primary outcome(s)
1. Maximum Observed Concentration (Cmax) of Giredestrant Measured Using Plasma Samples Taken at Multiple Timepoints from Day 1 up to Day 12 or Early Termination
2. Time to Maximum Observed Concentration (tmax) of Giredestrant Measured Using Plasma Samples Taken at Multiple Timepoints from Day 1 up to Day 12 or Early Termination
3. Area Under the Concentration-time Curve from Hour 0 to the Last Measurable Concentration (AUC0-t) of Giredestrant Measured Using Plasma Samples Taken at Multiple Timepoints from Day 1 up to Day 12 or Early Termination
4. Area Under the Concentration-time Curve Extrapolated to Infinity (AUC0-∞) of Giredestrant Measured Using Plasma Samples Taken at Multiple Timepoints from Day 1 up to Day 12 or Early Termination
5. Percentage of AUC Due to Extrapolation from the Last Measurable Concentration to Infinity (%AUCextrap) of Giredestrant Measured Using Plasma Samples Taken at Multiple Timepoints from Day 1 up to Day 12 or Early Termination
6. Apparent Terminal Elimination Half-life (t1/2) of Giredestrant Measured Using Plasma Samples Taken at Multiple Timepoints from Day 1 up to Day 12 or Early Termination
7. Apparent Total Clearance (CL/F) of Giredestrant Measured Using Blood Samples at Multiple Timepoints at Multiple Timepoints from Day 1 up to Day 12 or Early Termination Visit (Day 12)
8. Apparent Volume of Distribution During the Terminal Elimination Phase (Vz/F) of Giredestrant Measured Using Plasma Samples at Multiple Timepoints from Day 1 up to Day 12 or Early Termination
9. Fraction of Unbound Giredestrant (fu) Measured Using Plasma Samples at Multiple Timepoints from Day 1 up to Day 12 or Early Termination
10. Unbound Maximum Observed Concentration (Cmax,u) of Giredestrant Measured Using Plasma Samples at Multiple Timepoints from Day 1 up to Day 12 or Early Termination
11. Unbound Area Under the Concentration-time Curve of Giredestrant at Multiple Timepoints from Hour 0 to the Last Measurable Concentration (AUC0-t,u) Measured Using Plasma Samples from Day 1 up to Day 12 or Early Termination
12. Unbound Area Under the Concentration-time Curve Extrapolated to Infinity (AUC0-∞,u) of Giredestrant Measured Using Plasma Samples at Multiple Timepoints from Day 1 up to Day 12 or Early Termination
13. Unbound Apparent Total Clearance (CLu/F) of Giredestrant Measured Using Plasma Samples at Multiple Timepoints from Day 1 up to Day 12 or Early Termination
14. Unbound Apparent Volume of Distribution During the Terminal Elimination Phase (Vz,u/F) of Giredestrant Measured Using Plasma Samples at Multiple Timepoints from Day 1 up to Day 12 or Early Termination

Key secondary outcome(s)
1. Number of Participants with Adverse Events (AEs) from Screening to End of Study (Approximately 2.5 years)

2. Number of Participants with Severity of AEs Determined According to National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0 (NCI CTCAE v5.0) from Screening to End of Study (Approximately 2.5 years)

Completion date
02/12/2024

Eligibility

Key inclusion criteria
1. Females between 18 and 75 years of age, inclusive, of non-childbearing potential including non-pregnant, non-lactating, and postmenopausal
2. Females with body weight ≥45 kilograms (kg) and body mass index (BMI) ranging from 18.5 to 40 kilogram per meter square (kg/m^2), inclusive, at Screening
3. In good health (except for additional inclusion criteria specific to hepatic impaired participants)
4. Clinical laboratory evaluations within the reference range for the test laboratory, unless deemed not clinically significant by the investigator. It is acceptable to have clinical laboratory values outside the reference range, consistent with participants hepatic condition
5. Negative hepatitis panel (hepatitis B surface antigen and hepatitis C virus antibody) and negative human immunodeficiency virus (HIV) antibody screens

Additional inclusion criteria for participants with normal hepatic function:
6. Matched to participants with mild, moderate, or severe hepatic impairment in age (±10 years) and body weight (±15 %)
7. Alanine aminotransferase (ALT), Aspartate aminotransferase (AST) and bilirubin must be less than or equal to the upper limit of normal (ULN)
8. Estimated creatinine clearance ≥60 millileter per minute (mL/min) at Screening

Additional inclusion criteria for participants with hepatic impairment only:
9. Considered to have mild, moderate, or severe hepatic impairment and has been clinically stable for at least 1 month prior to Screening
10. Chronic (>6 months), stable (no acute episodes of illness within the previous 1 month prior to Screening due to deterioration in hepatic function) hepatic insufficiency with features of cirrhosis due to any etiology. Participants must also remain stable throughout the Screening period
11. Stable medication regimen for at least 1 month prior to Check-in (Day -1)
12. Estimated creatinine clearance ≥55 mL/min at Screening

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit

75 Years

Sex
Female

Key exclusion criteria
1. History of allergy to giredestrant or any of its excipients
2. History of stomach or intestinal surgery (including cholecystectomy) or resection that would potentially alter absorption and/or excretion of orally administered drugs
3. Malabsorption syndrome or other conditions that would interfere with enteral absorption
4. Absolute neutrophil count <1.3 × 10^9/L (1300/µL) at Screening
5. History of active or latent tuberculosis (TB), regardless of treatment history, or positive QuantiFERON® TB Gold test
6. The use of poppy seed-containing foods or beverages within 7 days prior to Check-in (Day -1), unless deemed acceptable by the investigator
7. The use of alcohol-, grapefruit-, or caffeine-containing foods or beverages within 72 hours prior to Check-in (Day -1), unless deemed acceptable by the investigator
8. Poor peripheral venous access
9. Female participant having a history of any malignancy, within 5 years prior to Screening, except for appropriately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, or Stage I uterine cancer
10. Evidence of infection with or positive test result for severe acute respiratory syndrome coronavirus 2

Additional exclusion criteria for participants with normal hepatic function:
11. Significant history or clinical manifestation of any metabolic, allergic, dermatological, hepatic, renal, hematological, pulmonary, cardiovascular, GI neurological, or psychiatric disorder (as determined by the investigator)
12. Regular alcohol consumption >14 units per week (1 unit = ½ pint beer or 25 mL shot of 40% spirit; 1.5 to 2 units = 125 mL glass of wine, depending on type) within 6 months prior to Screening

Additional exclusion criteria for participants with hepatic impairment only:
13. Minimal smoking (limit of less than 10 cigarettes/day) in hepatic impaired participants may be allowed at the discretion of the investigator and in consultation with the Sponsor and Medical Monitor. Participants will not be permitted to smoke within 2 hours prior to dose or 4 hours postdose on Day 1
14. Any evidence of progressive liver disease that has worsened or is worsening, as determined by the investigator, within 1 month prior to Screening
15. Demonstrated evidence of hepatorenal syndrome
16. Ascites requiring paracentesis (within 3 months prior to Check-in [Day -1]) or other intervention, with the exception of diuretics
17. Treatment for GI bleeding within 3 months prior to Check-in (Day -1)
18. Prescription of additional medication for hepatic encephalopathy within the 12 months (6 months for severe hepatic impairment) prior to Check-in (Day -1), unless deemed acceptable by the investigator
19. Total bilirubin levels >6 mg/dL. Levels above 6 mg/dL may be allowed at the discretion of the investigator, in consultation with the Sponsor and Medical Monitor
20. Hepatic encephalopathy Grade 2 or above

Date of first enrolment

15/10/2022

Date of final enrolment
24/10/2024

Locations

Countries of recruitment
United States of America

Study participating centre
Pinnacle Clinical Research
Anniston
United States of America
78215

Study participating centre
Orlando Clinical Research Center
Orlando
United States of America
32809

Study participating centre
Clinical Pharmacology of Miami
Miami, FL
United States of America
33014

Study participating centre
Inland Empire Clinical Trials
Rialto, CA
United States of America
92377

Sponsor information

Organisation
F. Hoffmann-La Roche Ltd

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to participant-level data not being a regulatory requirement.

IPD sharing plan summary
Not expected to be made available