ISRCTN38890848 https://doi.org/10.1186/ISRCTN38890848

A study to evaluate the processing by the body and safety of pralsetinib in participants with hepatic impairment compared to healthy participants

Submission date
29/10/2021

Recruitment status
No longer recruiting

Registration date
12/11/2021

Overall study status
Completed

Last Edited
12/11/2021

Condition category
Digestive System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims:
The purpose of this study is to measure how much of the study drug gets into the blood stream and how long it takes the body to get rid of it in participants with healthy livers compared to participants with moderate or severe liver impairment. In addition, this study will evaluate the safety and tolerability of the study drug in participants with healthy livers and participants with moderate or severe liver impairment. Information about any side effects that may occur will also be collected.

Who can participate?
Subjects aged between 18 to 74 years who are healthy, or have liver impairment.

What does the study involve?
During this study, participants have two visits, including a screening visit up to 34 days before the start of the study, and a stay in the study site lasting 10 days and 9 nights. The total duration of participation in the study will be about 10 days. In this study, the study doctor, and the sponsor will know the drugs and the doses that are given. Participants will be given a single oral (by mouth) dose of 200 mg pralsetinib given as 2 capsules on Day 1 given in the morning with one cup of water after an overnight fast (no food or drink other than water) of at least 8 hours. Then, it will be required to remain fasting for at least 2 hours after dosing (a total fast of at least 10 hours). One will not be allowed to drink water (except for the water given with dosing) from 1 hour before dosing to 2 hours after taking the capsules.
This study requires that a blood sample be obtained that may be used for additional research involving genetic analysis of blood. If participants do not wish to have this sample collected, will not be permitted to participate in this study. There is an additional research that may involve longterm storage for future analysis of blood for the Research Biosample Repository (RBR). Participants will be asked to sign a separate section of the informed consent for this additional research. If participants do not wish to participate in this additional research, the participation in this main research study will not be affected.

What are the possible benefits and risks of participating?
Participation in this study is purely for research purposes, and will not improve ones health or treat any medical problems. One may benefit by having physical examinations. The results of laboratory tests done at the screening visit will be made available upon request. However, if disqualified for study participation by other screening procedures, some laboratory tests may not be conducted.
Participants may have side effects from the drugs or procedures used in this study. Side effects can be mild to severe and even life threatening or fatal, and they can vary from person to person. Talk to the study doctor right away if one experiences any side effects during the study. There may be a risk in exposing an unborn child to study drug, and all risks are not known at this time. Women and men must take precautions to avoid exposing an unborn child to study drug, as described in Section 1.6. If participants are pregnant, become pregnant, or are currently breastfeeding, one cannot take part in this study.

Where is the study run from?
Genentech (United States)

When is the study starting and how long is it expected to run for?
April 2021 to June 2022

Who is funding the study?
Genentech, Inc (United States)

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

Contact information

Type(s)
Public

Contact name
Dr Clinical Trials

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

Additional identifiers

Protocol serial number
GP43163

Study information

Scientific Title

A Phase I, Open-Label, Single-Dose Study to Evaluate the Pharmacokinetics and Safety of Pralsetinib in Subjects With Moderate or Severe Hepatic Impairment Compared to Healthy Subjects

Study objectives
To evaluate the safety and tolerability of pralsetinib in participants with healthy livers and in participants with moderate or severe liver impairment

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 26/07/2021, Salus IRB (2111 W. Brake Lane, Suite 100, Austin, 78758, USA; +1 512-382-8902; salus@salusirb.com), ref: GP43163

Study design
Phase I multicenter single-dose open-label parallel-group study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Hepatic impairment

Interventions
Participants will be enrolled into one of three cohorts:
Cohort 1 (Participants with normal hepatic function)
Cohort 2 (Participants with moderate hepatic impairment), Child-Pugh score 7 to 9, inclusive, who show elevated bilirubin and decreased albumin levels
Cohort 3 (Participants with sever hepatic impairment), Child-Pugh score 10 to 15, inclusive, who show elevated bilirubin and decreased albumin levels

A single 200 mg oral dose of pralsetinib will be administered to fasted male and female participants with varying degrees of hepatic impairment on Day 1. Participants will be confined to the clinic until study completion (Day 9). After initiation of study drug administration, all adverse events will be reported until 14 days after the final dose.

Intervention Type
Drug

Phase
Phase I

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

Primary outcome(s)

Pharmacokinetic (PK) parameters of pralsetinib will be measured using blood samples on Day 1 at predose, 0.5, 1, 2, 3, 4, 6, 8, 12 h., Day 2 at 24 and 36 h., Day 3 at 48 h., Day 4 at 72 h., Day 5 at 96 h., Day 7 at 144 h. and Day 9 at 192 h.
The following PK parameters will be calculated if data allows:
1. Maximum concentration (Cmax)
2. Time to maximum observed concentration (Tmax)
3. Area under the concentration-time curve (AUC) from Hour 0 to the time of the last measurable concentration (AUC0-t)
4. AUC from Hour 0 to “t” (AUC0-“t”)
5. AUC extrapolated to infinity (AUC0-∞)
6. Percentage of AUC that is due to extrapolation from the last quantifiable concentration to infinity (%AUCextrap)
7. Apparent terminal elimination rate constant (λz)
8. Apparent terminal elimination half-life (t1/2)
9. Fraction of unbound drug (fu)
10. Cmax of free drug (Cmax,u)
11. AUC0-t of free drug (AUC0-t,u)
12. AUC0-“t” of free drug (AUC0-“t”,u)
13. AUC0-∞ of free drug (AUC0-∞,u)
14. Apparent total clearance (CL/F)
15. Apparent volume of distribution during the terminal elimination phase (Vz/F)

Key secondary outcome(s))
1. Incidence, nature and severity of adverse events with severity determined according to National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0 (NCI CTCAE v5.0), measured throughout the study.
2. Incidence of electrocardiogram (ECG) abnormalities as measured by 12-lead ECG at screening, days 1, 2 and 5 and at study completion.

Completion date
16/06/2022

Eligibility

Key inclusion criteria
1. Males or females of non-childbearing potential, between 18 and 74 years of age, inclusive
2. Normal hepatic function, moderate hepatic impairment, or severe hepatic impairment based on the Child-Pugh classification

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
74 years

Sex
All

Key exclusion criteria
1. History of surgical or artificial shunts (i.e., transjugular intrahepatic portosystemic procedure)
2. QT interval corrected using Fridericia's formula >480 ms demonstrated on at least two ECGs that are performed >30 minutes apart or history or presence of an abnormal ECG, which, in the investigator's opinion, is clinically significant
3. History of alcoholism or drug addiction within 1 year prior to Check-in (Day -1)
4. Use of oral antibiotics to treat an active infection within 4 weeks or intravenous antibiotics to treat an active infection within 8 weeks prior to Screening
5. Prior exposure to pralsetinib or other RET kinase inhibitor within 30 days prior to Check-in

Date of first enrolment
24/11/2021

Date of final enrolment
04/01/2022

Locations

Countries of recruitment
United States of America

Study participating centre
American Research Corporation Inc.
607 Camden Street, # Suit 101
San Antonio
United States of America
78215

Study participating centre
Orlando Clinical Research Center
5055 S Orange Avenue
Orlando
United States of America
32809

Study participating centre
Pinnacle Clinical Research - San Antonio
5109 Medical Drive, 3rd Floor

San Antonio
United States of America
78229

Study participating centre
Floridian Clinical Research Center
14791 Oak Lane
Miami Lakes
United States of America
33016

Sponsor information

Organisation
Roche (United States)

ROR
https://ror.org/011qkaj49

Funder(s)

Funder type
Industry

Funder Name
Genentech

Alternative Name(s)
Genentech, Inc., Genentech USA, Inc., Genentech USA

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

The datasets are not expected to be made available as there is no regulatory requirement to do so.

IPD sharing plan summary

Not expected to be made available