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A study to compare how much of divarasib is absorbed after a single oral dose of two different tablet formulations in healthy participants

Submission date
22/03/2024

Recruitment status
No longer recruiting

Registration date
28/03/2024

Overall study status
Completed

Last Edited
18/04/2024

Condition category
Other

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

Plain English summary of protocol

Background and study aims
Cancer is a disease caused when cells divide uncontrollably and spread into surrounding tissues. Changes or alterations in some genes can cause cancer or promote its growth. Despite significant breakthroughs in the understanding, prevention, and treatment of cancer, the disease continues to affect millions of people worldwide.
This study is testing a medicine called divarasib. It is being developed for the treatment of certain cancers. Divarasib is an experimental medicine. This means health authorities (like the US Food and Drug Administration and European Medicines Agency) have not approved divarasib for the treatment of cancer. Divarasib will be given to people by mouth as a single tablet or two tablets of the same dose under fasted conditions. This is to compare how much of the divarasib enters the blood and how long it takes for blood levels of divarasib to decrease with time.

Who can participate?
Healthy people (males and females) of 18-60 years of age can take part in the study. Females who are pregnant, have the potential to become pregnant, or are currently breastfeeding cannot take part in the study.

What does the study involve?
People will be screened to check if they can participate in the study. The screening period will take place about 28 days before the start of the treatment.
Everyone who joins this study will be split into 2 groups randomly (like flipping a coin) to receive divarasib in one of two treatment sequences.
Sequence 1: A single tablet of divarasib taken by mouth (orally) on an empty stomach followed by two tablets of divarasib taken orally after a period of 7 days.
Sequence 2: Two tablets of divarasib taken by mouth (orally) on an empty stomach followed by one single tablet of divarasib taken orally after a period of 7 days. Participants will have a 1:1 chance of being placed in any of the groups.
This is an open-label study. This means everyone involved, including the participant and the

study doctor, will know the study treatment the participant has been given.
During screening visit study participants will be required to stay at the clinic for 13 days and 12 nights (from check-in on Day -1 of Period 1 of the study to discharge on Day 5 of Period 2 of the study). Study doctors will check on the participants to see if there are any unwanted effects. Participants will have two follow-up visits on Days 14 and 28 of Period 2, during which the study doctor will check on the participant's well-being. The total duration of participation in the study will be about 5 weeks, not including the screening visit. Participants have the right to stop study treatment and leave the study at any time if they wish to do so.

What are the possible benefits and risks of participating?
Taking part in the study will not provide any benefit to healthy participants but the information collected in the study can help other people with health conditions in the future.
It may not be fully known at the time of the study how safe the study treatment is in healthy volunteers. The study involves some risks to the participant, but these risks are generally mild and easily monitored. People interested in taking part will be informed about the risks, as well as 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 side effects.
Participants may have unwanted effects of the drug 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.
Participants will be told about the known unwanted effects of divarasib and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines.

Where is the study run from?
Genentech (Switzerland)

When is the study starting and how long is it expected to run for?
October 2023 to May 2024

Who is funding the study?
Genentech (Switzerland)

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

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
GP45240

Study information

Scientific Title
A Phase I, open label, single dose, randomized, two-period crossover study to evaluate the relative bioavailability of single oral doses of two different formulations of divarasib (GDC-6036; 200-mg tablet and 400-mg tablet) in healthy subjects

Study objectives
The purpose of this study is to evaluate the relative bioavailability, safety, and tolerability of divarasib as one 400-milligram (mg) film-coated immediate-release (FCIR) tablet as compared to two 200-mg FCIR tablets in healthy adult participants.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 16/02/2024, Salus IRB (2111 W. Braker Lane Suite 100, Austin, Texas, 78758, United States of America; +1 (0)512 382 8902; salus@salusirb.com), ref: Nil

Study design
Phase I open-label single-dose randomized two-period crossover study

Primary study design
Interventional

Study type(s)
Other, Safety

Health condition(s) or problem(s) studied
Healthy participants

Interventions
Participants will be randomized according to a randomization schedule generated by a Fortrea biostatistician.

Treatment A, followed by treatment B: Participants will first receive divarasib, 400 mg as a single 400 mg tablet (treatment A), orally, under fasted conditions on Day 1 of Period 1. After a 7-day washout period, participants will then receive 400 mg of divarasib, as two tablets of 200 mg each (treatment B), orally, under fasted conditions on Day 1 of Period 2.

Treatment B, followed by treatment A: Participants will first receive 400 mg of divarasib, as two tablets of 200 mg each (treatment B), orally, under fasted conditions on Day 1 of Period 1. After

a 7-day washout period, participants will receive divarasib, 400 mg as a single 400 mg tablet (treatment A), orally, under fasted conditions on Day 1 of Period 2.

Intervention Type
Drug

Phase
Phase I

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

Primary outcome(s)
1. Pharmacokinetic (PK) parameters of divarasib measured using blood samples collected over 5 days on periods 1 and 2. The following PK parameters will be calculated if data allows:
1.1. Maximum observed concentration (Cmax) of divarasib measured using plasma concentration of divarasib collected over 5 days on period 1 and 2
1.2. Area under the concentration-time curve extrapolated to infinity (AUC 0-∞) of divarasib measured using plasma concentration of divarasib collected over 5 days on period 1 and 2
1.3. Area under the concentration-time curve from hour 0 to last measurable concentration (AUC 0-t) of divarasib measured using plasma concentration of divarasib collected over 5 days on period 1 and 2

Key secondary outcome(s))
1. Number of participants with adverse events (AEs) graded as per national cancer institute common terminology criteria for adverse events version 5.0 (NCI CTCAE; v5.0) from signing of informed consent up to Day 28 of Period 2 (approximately 5 weeks)

Completion date
08/05/2024

Eligibility

Key inclusion criteria
1. Males or females of non-childbearing potential
2. Body mass index (BMI) ranges from 18.0 to 32.0 kilogram per meter square (kg/m^2)
3. In good health, determined by no clinically significant findings from medical history, physical examination, triplicate 12-lead electro cardiogram (ECGs), and vital signs
4. Negative test for selected drugs of abuse at Screening (does not include alcohol) and at Check-in (Day -1 of Period 1) (does include alcohol)
5. Negative hepatitis panel (hepatitis B surface antigen, hepatitis B virus core antibody, and hepatitis C virus antibody) and negative Human Immunodeficiency Virus (HIV) antibody screens
6. Able to comply with the study protocol, including an overnight (at least 8 hours) fast before dosing

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
60 years

Sex
All

Key exclusion criteria
1. Significant history or clinical manifestation of any metabolic, allergic (to any drug compound, food, or other substance), dermatological, hepatic, renal, hematological, pulmonary, cardiovascular, gastrointestinal (GI) (stomach or intestinal surgery or resection), neurological, or psychiatric disorder
2. History of significant hypersensitivity, significant intolerance, or significant allergy to any drug compound, food, or other substance, unless approved by the investigator
3. Participation in any other investigational study drug trial in which receipt of an investigational study drug occurred within 5 half-lives or 30 days, whichever is longer, before Check-in (Period 1 Day -1)
4. Receipt of a coronavirus disease 2019 (COVID-19) vaccine in the past 28 days before Check-in (Period 1 Day -1)
5. Use of any prescription medications/products within 14 days prior to Check-in (Period 1 Day -1), unless deemed acceptable by the investigator
6. Serious infection requiring oral antibiotics within 4 weeks or intravenous (IV) antibiotics within 8 weeks of Screening
7. History of stomach or intestinal surgery or resection that would potentially alter absorption and/or excretion of orally administered drugs, except that appendectomy and hernia repair will be allowed

Date of first enrolment
08/03/2024

Date of final enrolment
04/04/2024

Locations

Countries of recruitment
United States of America

Study participating centre
Fortrea
United States of America
75230

Sponsor information

Organisation
Genentech

ROR
https://ror.org/04gndp242

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 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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes