ForPatients
by Roche

CancerHealthy Volunteers

A study to find out what happens to a new medicine (divarasib) inside the human body

A Phase I, open-label study of the absorption, metabolism, and excretion of [14C]-GDC-6036 following a single oral dose in healthy male subjects

Trial Status	Trial Runs In	Trial Identifier
Completed	1 Country	ISRCTN10152571 GP44415

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 1, open-label study of the absorption, metabolism, and excretion of [14C]-GDC-6036

Trial Summary:

Divarasib, an experimental medicine for cancer, is an inhibitor of the KRAS G12C protein, found in several cancers. This clinical trial was done to find out what happens to divarasib inside the human body. Healthy people received a single dose of divarasib that was tagged with a radiolabel. Researchers did tests to follow divarasib, its radiolabel, and its route of elimination from the body. They tested blood, feces, and urine samples. This was a phase 1, open-label study of the absorption, metabolism, and excretion of [14C]-divarasib.

Genentech, Inc. (A part of F. Hoffmann-La Roche Ltd., Switzerland)
Sponsor

Phase 1
Phase

ISRCTN10152571 GP44415
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
Male	18 to 65 years	Yes

Background and study aims

Healthy volunteers were enrolled at one study site in the USA to evaluate the pharmacokinetics, mass balance, and route of elimination for divarasib, a “KRAS G12C inhibitor” class of cancer medicine. Eight participants received radiolabeled divarasib. Results showed that after a single dose, most of the radiolabel (94%) was recovered within 120 hours. About 98% of the radiolabel was recovered in feces (95%) and urine (3%) within 840 hours after dosing.

GDC-6036 is an experimental drug being developed for the potential treatment of cancers with particular changes in the genes. An experimental drug is a drug that has not been approved by health authorities. The aim of this study is to:

1. Determine how the study drug is processed by and removed from the body.
2. Determine how much of the study drug gets into the blood, urine, and stool, and how long it takes the body to get rid of it.
3. Evaluate the study drug and its breakdown products in blood, urine, stool, and, for some participants, bile (a liquid that is made by the liver, stored in the gallbladder, and aids in digestion).
4. Evaluate how safe and tolerable the study drug is and collect information regarding its side effects.

Who can participate?

Male participants between 18 and 65 years

What does the study involve?

Participants will have to be a part of this study for a minimum of 15 days, and up to about 8.5 weeks, not including the screening visit. The study will have three parts:

first there is a screening period of up to 27 days before dosing wherein participants will undergo various tests to determine if they are eligible to participate in the study. Treatment/confinement: Eligible participants will be admitted to the study site (CRU) on the day prior to GDC-6036 dosing (check-in [Day -1]). During this period all participants will receive a single oral dose of 100 mg [14C]-GDC- 6036 capsule followed by 240 ml of room temperature water on Day 1 under fasted conditions. Participants will remain confined at the study site from the time of check-in (Day -1) until clinic discharge (at least Day 14 [312 hours after study drug administration (postdose)] if certain discharge criteria are met. Participants who do not meet the discharge criteria will have to remain in the study site for up to Day 28 [648 hours postdose]). If by Day 28, discharge criteria have not been met, the subject may be asked to return to the CRU every 7 days thereafter, for up to 4 times.

Follow-up: All participants will be followed up for any serious adverse events (SAEs), adverse events of special interest (AESIs) and pregnancies after the treatment is finished up to a maximum of Day 57 (±1 day).

What are the possible benefits and risks of participating?

Participation in this study is purely for research purposes and will not improve the health or treat any medical problem a participant may have, but the information that is learned may help people with certain kinds of cancers in the future. A participant may benefit by having physical examinations. The results of laboratory tests done at the screening visit will be made available to the participant upon request.

Participants will receive monetary compensation for participating in this study.
Participants may have side effects from the drug 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.

There may be a risk in exposing an unborn child to the study drug, and all risks are not known at this time. Participants must take precautions to avoid exposing an unborn child to the study drug.

The study drug GDC-6036 has had limited testing in humans.
Known/potential side effects: Loose stools (diarrhea), nausea, vomiting, fatigue, abnormal liver tests which may indicate liver damage, decreased appetite, headache, stomach pain (abdominal pain), increase in certain secretions of a gland called pancreas indicating pancreatic damage, acid reflux (gastroesophageal reflux disease), upset stomach (dyspepsia), constipation.
Unknown/Unforeseeable risks: Severe or life-threatening allergic reactions or unexpected interactions with another medication. Symptoms of an allergic reaction may include rash, flushing, itching, sneezing, or runny nose, abdominal pain, diarrhea, swelling of face, tongue or throat, dizziness, lightheadedness or fainting, trouble breathing, irregular or racing heart rate, and seizures.
The bile samples will be collected using the EnteroTracker® capsule and string device. Participants will have to swallow a gelatin capsule which contains the string within. The end of the string will be tapped to the participant's cheek or the back of their neck. The string will be pulled out after a specified period of time. During the string test participants may have an uncomfortable sensation due to the string in the back of their throat. They may also have trouble swallowing the pill. In addition, when the string is pulled back up, they may gag or feel like they want to vomit. The string is very small and thin and will likely not hurt the participant as it comes back up. The study staff will likely remove the string quickly, within a few seconds, which means that any discomfort should not last long. On rare occasions, a mild, superficial lesion caused by the string retrieval may result in some bleeding.

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

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

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

Inclusion Criteria:

- Male participants, between 18 and 65 years of age, inclusive
- Within body mass index (BMI) range 18.0 to 32.0 kilograms per meter square (kg/m^2), inclusive
- In good health, determined by no clinically significant findings from medical history, 12-lead electrocardiogram (ECG), and vital signs
- Clinical laboratory evaluations (including chemistry panel [fasted at least 8 hours], complete blood count [CBC], and urinalysis [UA] with complete microscopic examination) within the reference range for the test laboratory, unless deemed not clinically significant by the investigator
- Negative test for selected drugs of abuse at Screening
- 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
- Participants who have a history of a minimum of 1 bowel movement per day

Exclusion Criteria:

- History of stomach or intestinal surgery or resection that would potentially alter absorption and/or excretion of orally administered drugs
- Administration of a COVID-19 vaccine in the past 30 days prior to Screening
- History of malignancy, except for a history of 5 years or more of appropriately treated non-melanoma skin carcinoma
- Exposure to significant diagnostic or therapeutic radiation (e.g., serial X-ray, computed tomography scan, barium meal) or current employment in a job requiring radiation exposure monitoring within 12 months prior to Check-in (Day -1)
- Participation in more than three radiolabelled drug studies in the last 12 months (previous study to be at least 4 months prior to Check-in [Day -1] where exposures are known to the investigator or 6 months prior to Check-in [Day -1] for a radiolabelled drug study where exposures are not known to the investigator). The total 12-month exposure from this study and a maximum of two other previous radiolabelled studies within 4 to 12 months prior to this study will be within the CFR-recommended levels considered safe, per US Title 21CFR 361.1