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A study evaluating the absorption, metabolism, and excretion of [14C]-GDC-6036 following a single oral dose in healthy male participants

Submission date 13/03/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 17/03/2023	**Overall study status** Completed	
Last Edited 30/10/2023	**Condition category** Other	

Plain English summary of protocol

Background and study aims
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)

When is the study starting and how long is it expected to run for?
August 2022 to May 2023

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

Who is the main contact?
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Contact information

Type(s)
Public

Contact name
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Additional identifiers

Protocol serial number
GP44415

Study information

Scientific Title
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

Study objectives
The main aim of this study is to determine the mass balance, routes, and rates of elimination of total radioactivity following a single oral dose of [14C]-GDC-6036 in healthy male participants and characterizing the plasma pharmacokinetics (PK) of GDC-6036 as well as plasma and whole blood total radioactivity following a single oral dose of [14C]-GDC-6036 in healthy male participants.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/01/2023, Salus IRB (2111 W. Braker Lane Suite 100, Austin, Texas, 78758, USA; +1 (0)512 382 8902; salus@salusirb.com), ref: not applicable

Primary study design
Interventional

Study design
Single-center open-label non-randomized trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied

Absorption, metabolism, and excretion of [14C]-GDC-6036

Interventions
All participants will receive a single oral dose of [14C]-GDC-6036, 100 milligrams (mg) on Day 1 under fasted conditions.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
[14C]-GDC-6036

Primary outcome(s)
1. Concentration of GDC-6036 measured using a validated liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay on plasma samples from Day 1 up to Day 58
2. Concentration of total radioactivity measured using liquid scintillation counting on plasma, whole blood, urine and feces samples from Day 1 up to Day 58
3. Maximum observed concentration (Cmax) of GDC-6036 measured from plasma samples using model-independent approach at multiple timepoints from Day 1 up to Day 58
4. Time to maximum observed concentration (Tmax) of GDC-6036 measured from plasma samples using model-independent approach at multiple timepoints from Day 1 up to Day 58
5. Area under the concentration-time curve from hour 0 to the time of the last measurable concentration (AUC0-t) of GDC -6036 measured from plasma samples using model-independent approach at multiple timepoints from Day 1 up to Day 58
6. Time to the last measurable concentration (Tlast) of GDC-6036 measured from plasma samples using model-independent approach at multiple timepoints from Day 1 up to Day 58
7. Area under the concentration-time curve extrapolated to infinity (AUC0-∞) of GDC-6036 measured from plasma samples using model-independent approach at multiple timepoints from Day 1 up to Day 58
8. Apparent terminal elimination rate constant (λz) of GDC-6036 measured from plasma samples using model-independent approach at multiple timepoints from Day 1 up to Day 58
9. Apparent terminal elimination half-life (t1/2) of GDC-6036 measured from plasma samples using model-independent approach at multiple timepoints from Day 1 up to Day 58
10. Maximum observed concentration (Cmax) of total radioactivity measured from plasma and whole blood samples using model-independent approach at multiple timepoints from Day 1 up to Day 58
11. Time to maximum observed concentration (Tmax) of total radioactivity measured from plasma and whole blood samples using model-independent approach at multiple timepoints from Day 1 up to Day 58
12. Area under the concentration-time curve from hour 0 to the time of the last measurable concentration (AUC0-t) of total radioactivity measured from plasma and whole blood samples using model-independent approach at multiple timepoints from Day 1 up to Day 58
13. Time to the last measurable concentration (Tlast) of total radioactivity measured from plasma and whole blood samples using model-independent approach at multiple timepoints from Day 1 up to Day 58
14. Area under the concentration-time curve extrapolated to infinity (AUC0-∞) of total radioactivity measured from plasma and whole blood samples using model-independent approach at multiple timepoints from Day 1 up to Day 58

15. Apparent terminal elimination rate constant (λz) of total radioactivity from plasma and whole blood samples using model-independent approach at multiple timepoints from Day 1 up to Day 58
16. Apparent terminal elimination half-life (t1/2) of total radioactivity from plasma and whole blood samples using model-independent approach at multiple timepoints from Day 1 up to Day 58
17. Apparent total clearance (Cl/F) of GDC-6036 from plasma samples using model-independent approach at multiple timepoints from Day 1 up to Day 58
18. Apparent volume of distribution (Vz/F) of GDC-6036 from plasma samples using model-independent approach at multiple timepoints from Day 1 up to Day 58
19. Amount of total radioactivity excreted in urine (Aeu) measured using urine samples at multiple timepoints from Day 1 up to Day 58
20. Percentage of total radioactive dose excreted in urine (%Feu) measured using urine samples at multiple timepoints from Day 1 up to Day 58
21. Amount of total radioactivity excreted in feces (Aef) measured using fecal samples at multiple timepoints from Day 1 up to Day 58
22. Percentage of total radioactive dose excreted in feces (%Fef) measured using fecal samples at multiple timepoints from Day 1 up to Day 58
23. Amount of total radioactivity and percentage of total radioactive dose recovered in total excreta (faeces + urine) measured using urine and faecal samples from Day 1 up to Day 58

Key secondary outcome(s)
1. Percentages of GDC-6036 and detectable metabolites measured using plasma, bile, urine and faeces at multiple timepoints from Day 1 up to Day 58
2. Percentage of participants with adverse events (AEs) recorded from Day 1 up to Day 58
3. Apparent terminal elimination half-life (t1/2) of M21 metabolite measured using a validated liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay on plasma samples at multiple timepoints from Day 1 up to Day 58

Completion date
03/05/2023

Eligibility

Key inclusion criteria
1. Male participants, between 18 and 65 years of age, inclusive
2. Within body mass index (BMI) range 18.0 to 32.0 kilograms per meter square (kg/m^2), inclusive
3. In good health, determined by no clinically significant findings from medical history, 12-lead electrocardiogram (ECG), and vital signs
4. 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
5. Negative test for selected drugs of abuse at Screening
6. 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
7. Participants who have a history of a minimum of 1 bowel movement per day

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Male

Key exclusion criteria
1. History of stomach or intestinal surgery or resection that would potentially alter absorption and/or excretion of orally administered drugs
2. Administration of a COVID-19 vaccine in the past 30 days prior to Screening
3. History of malignancy, except for a history of 5 years or more of appropriately treated non-melanoma skin carcinoma
4. 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)
5. 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

Date of first enrolment
21/03/2023

Date of final enrolment
21/03/2023

Locations

Countries of recruitment
United States of America

Study participating centre
Labcorp Drug Development
3402 Kinsman Boulevard
Madison
United States of America
WI 53704

Sponsor information

Organisation
F. Hoffmann-La Roche (Switzerland)

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

Alternative Name(s)
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

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