ISRCTN10450075 https://doi.org/10.1186/ISRCTN10450075

A study to measure how much of the study drug GDC-6036 is absorbed and the effect of food on absorption in healthy participants

Submission date	Recruitment status	[ ] Prospectively registered
16/08/2021	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
27/08/2021	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
04/11/2021	Other	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
GDC-6036 is an experimental drug (not yet approved by health authorities) being developed for the treatment of non-small cell lung cancer (NSCLC), colorectal cancer, and other tumor types.
The aims of this study are:
1. To compare how much of the study drug is absorbed and how long it takes to get eliminated in two different forms of GDC-6036 (tablet and capsule)
2. To evaluate the effect food has on the absorption of the study drug in tablet form
3. To collect information on any side effects that may occur when the study drug is taken with food and/or without food

Who can participate?
Healthy male and female volunteers aged 18 to 60 years, inclusive

What does the study involve?
Participants will be given a single oral dose of GDC-6036 on Day 1 in each period. Within each period, they will receive GDC-6036 as either a capsule after fasting, as a tablet after fasting, or as a tablet after eating a high-fat breakfast, with about one cup of water. Participants will receive each dose regimen once. The order in which participants will receive the different dosing regimens will be determined randomly. There will be a washout period (a time in which no dosing is given) of 5 days between each dosing.
The study drug will be 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. In one of the dosing periods, participants will be required to eat a high-fat breakfast consisting of two eggs fried in butter, two strips of bacon, two slices of toast with butter, 4 ounces of hash brown potatoes, and a cup of whole milk. Participants will need to eat the entire breakfast within 25 minutes, and dosing will be given within 10 minutes after finishing the meal. Participants will be required to remain fasting for 4 hours after dosing (a total fast of 12 hours for the 2 periods without breakfast) and will not be allowed to drink water (except for the water given with dosing) from 1 hour before dosing to 2 hours after dosing.

What are the possible benefits and risks of participating?
Participants are not expected to receive any direct benefits from the study, but the information that is learned may help other people in the future. During the study, some side effects (unwanted effects or health problems) from the study drug or from the study procedures may be experienced. Some of the common side effects are diarrhea, nausea, vomiting, elevated liver enzymes in the blood, fatigue (feeling tired), constipation, headache, abdominal pain, anemia (decrease in red blood cells), cough, decreased appetite, and reduced potassium level in the blood. There may also be a risk in exposing an unborn child to the study drug - the risks for this are not yet known. There may also be unknown, infrequent, and unforeseeable risks associated with the use of the study drug including severe or life-threatening allergic reactions or unexpected interactions with another medication.

Where is the study run from?
Genentech, Inc (USA)

When is the study starting and how long is it expected to run for?
January 2021 to October 2021

Who is funding the study?
Genentech, Inc (USA)

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

Contact information

Type(s)
Public

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
GP43039

Study information

Scientific Title
A Phase I, open-label, single-dose, randomized, three-period crossover study to evaluate the relative bioavailability and food effect of GDC-6036 in healthy subjects

Study objectives
To evaluate the relative bioavailability and food effect of GDC-6036 in healthy participants.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 18/06/2021, Salus Institutional Review Board (IRB) (2111 W. Braker Lane, Suite 100, Austin, Texas, 78758, USA; +1 (0)512 382 8902; salus@salusirb.com), ref: GP43039

Study design
Phase I single-centre open-label randomized crossover study

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Bioavailability and food effect of GDC-6036 in healthy subjects

Interventions
GDC-6036 will be administered to healthy participants to determine the relative bioavailability of the film-coated immediate release (FCIR) tablet formulation compared to the Phase I powder in capsule (PiC) formulation in the fasted state. It will also determine the effect of food on the GDC-6036 tablet formulation.

Participants will be randomly assigned to one of three treatment sequences (ABC, BCA, and CAB) according to a randomization schedule generated by a Lapcorp Biostatistician which are outlined below:

Treatment A: a single oral dose of GDC-6036 capsule given with approximately one cup of room temperature water after at least an 8-hour fast, followed by at least a 4-hour fast postdose from food.
Treatment B: a single oral dose of GDC-6036 tablet given with approximately one cup of room temperature water after at least an 8-hour fast, followed by at least a 4-hour fast postdose from food.
Treatment C: a single oral dose of GDC-6036 tablet given with approximately one cup of room temperature water after at least an 8-hour fast. A high-fat breakfast meal will be started 30 minutes prior to dose and consumed over a 25-minute interval to ensure that the dose will be administered within 10 minutes after completing the meal, followed by at least a 4-hour fast postdose from food.

Treatments will be administered by mouth on Day 1 of Periods 1, 2 and 3.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
GDC-6036

Primary outcome measure
Pharmacokinetic (PK) parameters of GDC-6036 measured using blood samples at predose, 0.25, 0.50, 0.75, 1, 2, 3, 4, 6, 8, 12 h on day 1 of periods 1, 2 and 3; at 24 and 30 h on day 2 of periods 1, 2 and 3; at 48 and 56 h on day 3 of periods 1, 2 and 3; at 72 h on day 4 of periods 1, 2 and 3. The following PK parameters will be calculated if data allows:
1. Maximum concentration (Cmax) of GDC-6036 measured using plasma concentrations of GDC-6036
2. Time to maximum observed concentration (tmax) of GDC-6036 measured using plasma concentrations of GDC-6036
3. Time to first quantifiable concentration (tlag) measured using plasma concentrations of GDC-6036
4. Time of last quantifiable concentration (tlast) measured using plasma concentrations of GDC-6036
5. Area under the concentration-time curve from Hour 0 to the time of last quantifiable concentration (AUC0-t) measured using plasma concentrations of GDC-6036
6. Area under the concentration-time curve extrapolated to infinity (AUC0-inf) measured using plasma concentrations of GDC-6036
7. Percentage of AUC that is due to extrapolation from the last quantifiable concentration to infinity (%AUCextrap)
8. Apparent terminal elimination rate constant (λz)
9. Apparent terminal elimination half-life (t1/2)
10. Apparent total clearance (CL/F)
11. Apparent volume of distribution during the terminal elimination phase (Vz/F)

All measured at:
Day 1 of periods 1, 2 and 3 at predose, 0.25, 0.50, 0.75, 1, 2, 3, 4, 6, 8, 12 h

Day 2 of periods 1, 2 and 3 at 24 and 30 h
Day 3 of periods 1, 2 and 3 at 48 and 56 h
Day 4 of periods 1, 2 and 3 at 72 h

Secondary outcome measures
1. Frequency 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), recorded throughout the study
2. Incidence of abnormalities in clinical laboratory test results, measured by the evaluation of blood and urine tests at screening, check-in, days 1 and 2 of periods 1, 2 and 3 and at study completion
3. Incidence of electrocardiogram (ECG) abnormalities as measured by triplicate 12-lead ECG at screening, check-in, day 1 of periods 1, 2 and 3 at predose, 1, 2, 3, 4, 6, 8, 12 h; day 2, periods 1, 2 and 3 at 24 h and at study completion
4. Incidence of abnormalities in vital signs (blood pressure, pulse and oral temperature measured by an automated device and respiration rate measured manually by counting the rise and fall of the subject's chest for 30 seconds and multiplying by 2) measured at screening, check-in, day 1 of periods 1, 2 and 3 at predose, 1, 2, 3, 4, 6, 8, 12 h; day 2, periods 1, 2 and 3 at 24 h and at study completion
5. Physical examination conducted at check-in and at study completion

Overall study start date
31/01/2021

Completion date
11/10/2021

Eligibility

Key inclusion criteria
1. Males or females of non-childbearing potential, between 18 and 60 years of age, inclusive
2. Within body mass index (BMI) range 18.0 to 32.0 kg/m², inclusive
3. In good health, determined by no clinically significant findings from medical history, physical examination, triplicate 12-lead 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 HIV antibody screens
6. Able and willing to consume 100% of a high-fat breakfast meal (two eggs fried in butter, two strips of bacon, two slices of toast with butter, 4 ounces of hash brown potatoes, and 8 ounces of whole milk)
7. Receive an explanation of the mandatory whole genome sequencing component of the study

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
18

Key exclusion criteria
1. Significant history or clinical manifestation of any metabolic, allergic, dermatological, hepatic, renal, hematological, pulmonary, cardiovascular, gastrointestinal, neurological, or psychiatric disorder (as determined by the Investigator)
2. History of significant hypersensitivity, intolerance, or allergy to any drug compound, food, or other substance, unless approved by the Investigator
3. 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
4. History or presence of an abnormal ECG, which, in the Investigator's opinion, is clinically significant
5. Have a QTc interval corrected for heart rate using Fridericia's formula >450 msec for males, >470 msec for females, PR interval >210 msec, or QRS complex >120 msec. Triplicate ECGs will be performed at Screening and at Check-in and the mean value of the 3 measurements will be used. If intervals are out of range, ECGs may be repeated once at Screening and once at Check-in, and the average of the intervals will be used to determine eligibility
6. History of alcoholism or drug addiction within 1 year prior to Check-in (Day -1 of Period 1)
7. 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
8. Receipt of a coronavirus disease 2019 (COVID-19) vaccine in the past 28 days prior to dosing
9. Use of any prescription medications/products within 14 days prior to Check-in (Day -1 of Period 1), unless deemed acceptable by the Investigator
10. Use of any over-the-counter, non-prescription preparations (including vitamins; minerals; and phytotherapeutic-, herbal-, and plant-derived preparations) within 7 days prior to Check-in (Day -1 of Period 1), unless deemed acceptable by the Investigator
11. Use of tobacco- or nicotine-containing products (including, but not limited to, cigarettes, e-cigarettes, pipes, cigars, chewing tobacco, nicotine patches, nicotine lozenges, or nicotine gum) within 3 months prior to Check-in (Day -1 of Period 1) and during the entire study
12. Use of poppy seed-, grapefruit-, star fruit-, pomegranate-, pawpaw-, or Seville orange-containing foods or beverages within 7 days prior to Check-in (Day -1 of Period 1) and until completion of Period 3, unless deemed acceptable by the Investigator
13. Use of alcohol-containing foods or beverages within 48 hours prior to Check-in (Day -1 of Period 1) and until completion of Period 3
14. Use of caffeine-containing foods or beverages within 48 hours prior to Check-in (Day -1 of Period 1) and until completion of Period 3, unless deemed acceptable by the Investigator
15. Participation in strenuous exercise from 48 hours prior to Check-in (Day -1 of Period 1) and during the period of confinement at the study site (e.g., will not begin a new exercise program or participate in any unusually strenuous physical exertion)
16. Poor peripheral venous access
17. History of malignancy, except for appropriately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, or Stage I uterine cancer
18. Donation of blood from 30 days prior to Screening through Study Completion/ET, inclusive, or of plasma from 2 weeks prior to Screening through Study Completion/ET, inclusive
19. Receipt of blood products within 2 months prior to Check-in (Day -1 of Period 1) and during

the entire study duration
20. Serious infection requiring oral antibiotics within 4 weeks or intravenous antibiotics within 8 weeks of Screening
21. Any acute or chronic condition that, in the opinion of the Investigator, would limit the subject' s ability to complete and/or participate in this clinical study

Date of first enrolment
25/08/2021

Date of final enrolment
11/10/2021

Locations

Countries of recruitment
United States of America

Study participating centre
Labcorp Clinical Research Unit
1341 West Mockingbird Lane
Suite 200E
Dallas
United States of America
75247

Sponsor information

Organisation
Genentech, Inc.

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Sponsor type
Industry

Website
https://www.roche.com/about_roche/roche_worldwide.htm

Funder(s)

Funder type
Industry

Funder Name
Genentech

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

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
11/10/2022

Individual participant data (IPD) sharing plan
The datasets are not expected to be made available due to there being no regulatory requirement to do so.

IPD sharing plan summary
Not expected to be made available