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# A study to investigate the absorption, metabolism, excretion, and bioavailability of oral and intravenous inavolisib in healthy volunteers

**Submission date**
02/04/2021

**Recruitment status**
No longer recruiting

**Registration date**
04/05/2021

**Overall study status**
Completed

**Last Edited**
29/04/2021

**Condition category**
Cancer

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

## Plain English summary of protocol

Background and study aims
Breast cancer is the most commonly diagnosed cancer in women, with an estimated global incidence of 2,088,849 new cases and 626,679 deaths reported in 2018. Current treatments for advanced or metastatic disease focus on prolonging life and improving or maintaining quality of life. Preventing resistance to therapy and ultimately achieving a cure remain unmet needs in this disease setting.

Standard-of-care treatment options for patients with de novo metastatic disease, or for whom disease recurs following surgery and adjuvant treatment, include endocrine therapy, endocrine and targeted therapy combinations, or chemotherapy. For most patients, endocrine therapy alone or in combination with a targeted therapy is the treatment of choice in the metastatic setting.

Inavolisib as a single agent, or inavolisib in combination with other anti-cancer therapies, is being developed by Roche, for the treatment of locally advanced tumors or solid tumors with the PIK3CA-mutatation that have spread to other sites, including breast cancer. The development of inavolisib as a single agent and in various other combinations for other indications beyond breast cancer is ongoing.

This study will investigate the absorption, metabolism, excretion, and bioavailability of inavolisib in healthy volunteers. Information on the amount of active inavolisib available to the body using the current method of taking the drug will be helpful to plan future studies and may be useful to interpret data from these studies on how inavolisib moves through and interacts with the body. The results from this study may guide future study designs using special populations or evaluating the potential for drug-drug interactions.

Who can participate?
Up to 8 healthy male and female volunteers aged 18 to 65 years. Male volunteers are limited to 3 volunteers or less.

What does the study involve?
Participants will receive a single dose (9 mg) of inavolisib as a capsule taken by mouth in a fasted state. After 2 h 58 min, participants will receive a single intravenous infusion (100 µg) of inavolisib. Participants will be followed up for collection of blood, urine, and fecal samples over the following 336 h period.

What are the possible benefits and risks of participating?
High blood sugar, inflammation or ulcers of the mouth, rash, and diarrhea have been identified as risks for people receiving inavolisib treatment. These risks may require either stopping or reducing the dose of inavolisib and may have the potential to cause life-threatening conditions. Therefore, close monitoring and a robust risk-mitigation strategy will be used during this study. Results in previous studies have shown the inavolisib is well tolerated and there are no additional safety concerns beyond those associated with expected toxicities and effects of this class of drugs.

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

When is the study starting and how long is it expected to run for?
From November 2020 to April 2021

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

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

# Contact information

### Type(s)
Scientific

### Contact name
Dr Clinical Trials

### Contact details
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# Additional identifiers

### Clinical Trials Information System (CTIS)

Nil known

### ClinicalTrials.gov (NCT)
Nil known

### Protocol serial number
Sponsor reference GP42652

# Study information

### Scientific Title
A phase 1, open-label, single-center study to investigate the absorption, metabolism, excretion, and absolute bioavailability of a single oral dose of [14C]-labeled inavolisib and an iv tracer dose of [13C6]-labeled inavolisib in a single cohort of healthy volunteers

### Study objectives
To investigate the absorption, metabolism, excretion, and absolute bioavailability of Inavolisib in healthy volunteers

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approved 09/02/2021, Salus IRB (2111 W. Braker Lane, Suite 100, Austin, Texas 78758, USA; +1 512-380-1244; salus@salusirb.com), ref: GP42652

### Study design
Phase 1 single-center open-label non-randomized study

### Primary study design
Interventional

### Study type(s)
Treatment

### Health condition(s) or problem(s) studied
The absorption, metabolism, excretion, and bioavailability of a PI3K inhibitor drug in healthy volunteers

### Interventions
The participants will each receive a single 9 mg (approximately 200 µCi) oral capsule dose of [14C]-inavolisib administered in a fasted state and followed after 2 h 58 min by a single 100 µg intravenous (IV) dose of [13C6]-inavolisib administered as an IV push over 2 min. Participants will be followed up for regular collection of blood, urine, and fecal samples over a 336 h period.

### Intervention Type
Drug

### Phase
Phase I

### Drug/device/biological/vaccine name(s)
inavolisib

### Primary outcome(s)
1. Maximum concentration (Cmax) of inavolisib measured using the plasma concentrations of inavolisib and total radioactivity concentrations in plasma and whole blood from blood samples collected at 0 and 336 h
2. Area under the curve (AUC) of inavolisib measured using the plasma concentrations of inavolisib and total radioactivity concentrations in plasma and whole blood from blood samples collected at 0 and 336 h
3. Bioavailability of inavolisib measured using the plasma concentrations of inavolisib and total radioactivity concentrations in plasma and whole blood from blood samples collected at 0 and 336 h

### Key secondary outcome(s))
Percentage of the total radioactive dose excreted over the sampling interval and cumulatively across sampling intervals measured from urine and in fecal samples collected between 0 and 336 h

### Completion date
23/04/2021

## Eligibility

### Key inclusion criteria
1. Males, who are sterile, and females of non-childbearing potential
2. Aged between 18 and 65 years, inclusive
3. ≤3 male volunteers
4. Body mass index (BMI) between 18.5 and 32.0 kg/m², inclusive
5. In good health, determined by no clinically significant findings from medical history, 12-lead ECG, vital signs, and taking no chronic medications
6. Clinical laboratory evaluations within the reference range for the test laboratory, unless deemed not clinically significant by the Investigator. Evaluations will include a chemistry panel (fasted at least 8 h), complete blood count, coagulation testing (including prothrombin time, international normalized ratio, and activated partial thromboplastin time), and urinalysis with complete microscopic analysis, and glycosylated hemoglobin.
7. Negative test for selected drugs of abuse (does not include alcohol) at screening visit and day -1 (including alcohol)
8. Negative hepatitis panel (hepatitis B surface antigen and hepatitis C virus antibody) and negative human immunodeficiency virus (HIV) antibody screens
9. Negative screening test for latent mycobacterium tuberculosis (TB) infection using QuantiFERON® TB Gold
10. Receive an explanation of the mandatory WGS component of the study
11. Able to comprehend and willing to sign an Informed Consent Form (ICF)
12. History of ≥1 bowel movement per day
13. Male volunteers: sterile by history for at least 90 days prior to dosing, including volunteers who are sterile due to vasectomy, bilateral orchiectomy, other surgical procedure, or known sterilizing medical condition. Male volunteers should use a barrier method such as a condom with any female partner of child-bearing potential and with any pregnant partner for 90 days after dosing.

## Participant type(s)
Healthy volunteer

## Healthy volunteers allowed
No

## Age group
Adult

## Lower age limit
18 years

## Sex
All

## Total final enrolment
8

## Key exclusion criteria
1. History of type 1 diabetes or type 2 diabetes requiring systemic treatment
2. More than 1 of the following risk factors
2.1. BMI >32.0 kg/m²
2.2. Fasting blood glucose≥125 mg/dl (7.0 mmol/l)
2.3. Glycosylated hemoglobin (HbA1C) ≥6.5%
3. Have a PR interval >210 ms, QRS complex >120 ms, or QTc interval >450 ms for males, >470 ms for females
4. History or presence of an abnormal ECG that, in the Investigator's opinion, is clinically significant
5. Significant history or clinical manifestation of any metabolic, allergic, dermatological, hepatic, renal, hematological, pulmonary, cardiovascular, gastrointestinal (GI), neurological, or psychiatric disorder (as determined by the Investigator)
6. History of significant hypersensitivity, intolerance, or allergy to any drug compound, food, or other substance, unless approved by the Investigator
7. History of stomach or intestinal surgery or resection that would potentially alter absorption and/or excretion of orally administered drugs with the exception of appendectomy and hernia repair surgery
8. History of inflammatory bowel disease (such as Crohn's disease or ulcerative colitis), or active bowel inflammation (such as diverticulitis, with the exception of inactive diverticulosis)
9. History of ocular or intraocular conditions (such as cataract or diabetic retinopathy), active vitritis, history of or active uveitis, or active infections in the eye
10. History of alcoholism or drug addiction within 1 year prior to day -1
11. History of active or latent TB, regardless of treatment history
12. Participation in any other investigational study drug trial in which receipt of an investigational study drug occurred within 5 half-lives of the investigational agent or 30 days before screening whichever is longer
13. Receipt of the first or second dose of a Coronavirus Disease 2019 (COVID-19) vaccine given Emergency Use Approvals (US) or approved COVID-19 vaccine in the past 7 days prior to dosing or planned to receive any COVID-19 vaccines during the trial
14. History of active viral, bacterial, or fungal infection requiring IV treatment with antibiotics within 14 days prior to day -1
15. Use of any immunosuppressive therapies within 8 weeks prior to the Screening evaluation

16. Use of any prescription medications/products within 14 days prior to day -1, unless deemed acceptable by the Investigator
17. Use of any over-the-counter, non-prescription preparations (including vitamins; minerals; and phytotherapeutic-, herbal-, and plant-derived preparations) within 7 days prior to day -1, unless deemed acceptable by the Investigator
18. Use of any drugs known to be strong inhibitors or inducers of cytochrome P450 (CYP)3A, from within 30 days prior to day -1 until Study Completion
19. 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) from within 6 months prior to day -1 until Study Completion
20. Use of alcohol-, grapefruit-, or caffeine-containing foods or beverages from within 72 h prior to day -1 until Study Completion, unless deemed acceptable by the Investigator
21. Participation in strenuous exercise (a new exercise program or participation in any unusually strenuous physical exertion) from 48 h prior to day -1 and during the period of confinement at the study site
22. Poor peripheral venous access
23. History of malignancy, except for appropriately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, ductal carcinoma in situ of breast, or Stage I uterine cancer
24. Donation of blood from 30 days prior to Screening through Study Completion, Clinic Discharge, or Early Termination, inclusive, or of plasma from 2 weeks prior to Screening through Study Completion, Clinic Discharge, or Early Termination, inclusive
25. Receipt of blood products within 2 months prior to day -1
26. Any clinically significant deviations from normal ranges in coagulation factors
27. Any acute or chronic condition that, in the opinion of the Investigator, would limit the volunteer’s ability to complete and/or participate in this clinical study
28. 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 day -1
29. Participation in more than three radiolabeled drug studies in the last 12 months
30. Volunteers who, in the opinion of the Investigator (or designee), should not participate in this study
31. Female volunteers: pregnant, lactating, breastfeeding, or of childbearing potential

### Date of first enrolment
12/03/2021

### Date of final enrolment
09/04/2021

## Locations

### Countries of recruitment
United States of America

### Study participating centre
### Covance Clinical Research Unit, Inc
3402 Kinsman Blvd

Madison
United States of America
53704

# Sponsor information

**Organisation**
Genentech, Inc

# 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 this being a voluntary posting.

**IPD sharing plan summary**
Not expected to be made available