ForPatients
by Roche

Healthy Volunteers

A study to compare two different forms of a study medicine (belvarafenib), and look at the effect of food and stomach acid

A phase I, single-dose, randomized, crossover, relative bioavailability and food-effect study and phase I, single-dose, fixed-sequence, crossover, pH-effect study of belvarafenib (GDC-5573) in healthy subjects

Trial Status	Trial Runs In	Trial Identifier
Completed	1 Countries	GP44112

The source of the below information is the publicly available website ClinicalTrials.gov. It has been summarised and edited into simpler language.

Trial Summary:

This clinical trial studied belvarafenib, a cancer medicine, to understand how well it gets absorbed into blood under different conditions. Researchers tested two formulations of the medicine and examined the effects of food and stomach acid on its absorption. This Phase 1 study was conducted in healthy volunteers to help determine the best way to take a dose of belvarafenib for it to be an effective cancer treatment.

Genentech, Inc. (A part of F. Hoffmann-La Roche Ltd., Switzerland)	**Phase 1**
Sponsor	Phase

GP44112
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	18-65 years	Yes

When a medicine is taken by mouth, sometimes less than 100% is absorbed into the blood. Researchers looked at this “bioavailability” of belvarafenib, a cancer medicine. The study took place at one study site in the USA. They found exposure to the medicine in blood was similar for two different formulations. The study involved 74 healthy volunteers, and 26% experienced non-serious side effects related to belvarafenib. Findings from this study helped optimize dosing and highlight the impact of food and stomach acid on the effectiveness of this medicine.

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Background and study aims:

Belvarafenib (the study drug) is an experimental drug being developed for the treatment of certain types of cancer. Belvarafenib being an experimental drug is not yet approved by the health authorities. This study will be conducted in two parts. The purpose of this study is:

Part 1: This part of the study will compare the amount of study drug that enters the circulation of the body (to have an active effect), and how long it takes for the body to get rid of it when given as the original reference tablet formulation (belvarafenib di-hydrochloride salt [HCl]) compared to a new tablet formulation (belvarafenib bis-methanesulfonic acid salt [MSA] formulation), as well as the new tablet formulation given at different doses. Both formulations will be given with a low-fat meal.

Part 2: Food Effect: Part 2 of this study aims to evaluate the effect of food on the absorption of the new tablet formulation of the study drug, and to collect information on any side effects that may occur when the study drug (new tablet formulation) is taken with and without food.

Part 2: pH Effect: The purpose of this part of the study is to assess the effect of rabeprazole (an approved medication that changes the pH in the stomach) on the amount of study drug (new tablet formulation) that reaches the bloodstream, and how long the body takes to get rid of it, when given with a low-fat meal.

Both Part 1 & Part 2: The safety and tolerability of the study drug will be evaluated in both parts of the study.

Who can participate?

Healthy people aged between 18 to 65 years old

What does the study involve?

The study includes the following parts: Part 1, Part 2 (food effect), and Part 2 (pH effect). Participants will be enrolled in any one part of the study i.e., Part 1, Part 2 (food effect), and Part 2 (pH effect). Both parts of this study have 3 stages:

1. Screening: To see if participants are eligible for the study. Participants will have one clinic visit for screening which will be done 35 days before the first dose of the study drug.

2. Dosing/Confinement: Participants will receive study drugs during this period.

Part 1: Participants will be randomly assigned to one of the two groups, each having two dosing periods. The order in which the participants receive each dosing will be determined by chance.

Group 1a: Participants will receive a single dose of belvarafenib new formulation and original formulation by mouth, after a low-fat breakfast, on Day 1 of Period 1 and Day 1 of Period 2 in one of the two sequences:

Sequence I: Belvarafenib new formulation in Period 1 and belvarafenib original formulation in Period 2

Sequence II: Belvarafenib original formulation in Period 1 and Belvarafenib new formulation in Period 2

Group 1b: Participants will receive a single dose of 50 mg and 200 mg belvarafenib tablets (new formulation) by mouth, after a low-fat breakfast on Day 1 of Periods 1 and 2 in one of the two sequences:

Sequence I: Belvarafenib 50 mg, in Period 1 and belvarafenib 200 mg in Period 2

Sequence II: Belvarafenib 200 mg in Period 1 and belvarafenib 50 mg in Period 2

Part 2: Food effect: Participants will receive a single dose of belvarafenib new formulation by mouth on Day 1 of Period 1 and 2, in one of the two sequences. The order in which the participants receive each dosing will be determined by chance.

Sequence I: Belvarafenib with high-fat breakfast in Period 1 and belvarafenib without breakfast in Period 2.

Sequence II: Belvarafenib without breakfast in Period 1 and belvarafenib with high-fat breakfast in Period 2

Part 2: pH effect: Participants will receive a single dose of belvarafenib new formulation by mouth on Day 1 of Period 1. In Period 2, participants will receive a rabeprazole tablet by mouth on Days 1 to 5 and belvarafenib new formulation on Day 1 after a low-fat breakfast.

During this study, each dose of the medicines will be given in the morning after an overnight fast of at least 8 hours.

Participants will have to be a part of this study for 8 weeks (Part 1) and 7 weeks (Part 2: Food effect and pH effect), not including the screening visit. Participants will have to check in to the study site one day prior to belvarafenib dosing for both parts. There will be 2 clinic confinements visits for each part are as follows:

- Part 1: Clinic confinements of 11 days/10 nights

- Part 2 food effect: Clinic confinements of 11 days/10 nights

- Part 2 pH effect: One confinement lasting 11 days/10 nights; One clinic confinement lasting 15 days/14 night

There will be at least 18 days between each dosing in all the parts of the study.

3. Follow-up: To check on the participants after dosing is finished. Participants will have one outpatient visit 21 to 27 days after the last dose of the study drug for both Part 1 and Part 2 (food and pH effect). A follow-up phone call will be done only if the outpatient visit occurs between 21 and 27 days after the last dose of the study drug.

What are the possible benefits and risks of participating?

Participants will not receive any health benefits from participating in this study, but the information that is learned may help people with cancer in the future.

Participants may have side effects from the drugs used in this study. The known side effects of this drug, as well as potential side effects, are listed below.

Risks associated with belvarafenib:

1. Known Side Effects: Skin changes including different types of rashes and itching

2. Potential Side effects: Injury to the digestive tract, decreased heart function, abnormal electrical conduction within the heart, sensitivity to sunlight, acne, hair loss, constipation, nausea, or the urge to vomit, vomiting, heartburn, fatigue or tiredness, fever, loss of appetite, muscle pain, high blood pressure, severe skin or mucosal reactions, nerve injury, liver injury, kidney injury

Risks Associated with Rabeprazole: Abdominal pain, sore throat, gas, increased chance of infections, constipation.

There may be a risk in exposing an unborn child to study the drug, and all risks are not known at this time. Women who are pregnant, become pregnant, or are currently breastfeeding, cannot participate in this study.

Where is the study run from?

F. Hoffmann-La Roche Ltd (USA)

Who is funding the study?

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F. Hoffmann-La Roche Ltd (USA)

Who is the main contact?

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