ForPatients
*by Roche*

Solid Tumors

# A study to evaluate the safety, tolerability, processing by the body and effectiveness against BRAF-mutated solid tumours or melanoma of RO7276389 by itself or in combination with cobimetinib

A phase IA/B open-label study to evaluate safety, pharmacokinetics, and preliminary clinical activity of RO7276389 alone and in combination with cobimetinib in participants with Braf-V600 mutation-positive advanced solid tumor or Braf-V600 mutation-positive melanoma with central nervous system metastases

| Trial Status | Trial Runs In | Trial Identifier |
|---|---|---|
| Not Yet Recruiting | 1 Countries | WP43295 |

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

## *Trial Summary:*

The aim of this open-label study is to evaluate the safety, tolerability, processing by the body and effectiveness against BRAF-mutated solid tumours or melanoma of RO7276389 by itself or in combination with cobimetinib

**F. Hoffmann-La Roche (USA)**
Sponsor

**WP43295**
Trial Identifiers

## *Eligibility Criteria:*

| Gender | Age | Healthy Volunteers |
|---|---|---|
| Both | >= 18 years | No |

The purpose of the study is to test an experimental drug called RO7276389 when given by itself or in combination with another drug called cobimetinib in participants with solid tumours. Some solid tumours will have a change in a gene which in turn causes an abnormal change (mutation) in a protein called the BRAF protein. This changed BRAF protein will change the communication within the cells and hence can cause cancer. The existing cancer medicines that block the changed BRAF protein are less effective in cancers that spread to the brain. RO7276389 is an experimental drug that by itself, or in combination with cobimetinib, has been approved by health authorities for the treatment

of BRAF-mutant advanced cancer in participants in a clinical study. Cobimetinib is an anticancer medicine that blocks a protein called MEK which helps cancer cells to grow.

**The aims of the study are:**

- To find out the highest dose that a participant can tolerate and/or the recommended dose of RO7276389 by itself or in combination with cobimetinib.
- To find out how safe RO7276389 by itself or in combination with cobimetinib at different doses will be and to find out what side-effects this treatment may cause
- To find out if RO7276389 by itself or in combination with cobimetinib is effective against BRAF-mutated solid tumours or melanoma (a type of skin cancer).
- To find out how RO7276389 by itself or in combination with cobimetinib will be distributed and eliminated from the body.
- To find out the effect of food on the distribution and elimination of RO7276389 alone or in combination with cobimetinib from the body.

**Who can participate?** Participants who are over 18 years of age and have BRAF-mutated solid tumours.

**What does the study involve?** Participants may be asked to be in the study for up to 24 months. This includes:

- A Screening period of up to 28 days before the start of the study where tests will be done to check if the participants are eligible to take part in the study.
- Treatment period where participants will receive RO7276389 alone or in combination with cobimetinib daily in 4-week cycles. Participants will get the study treatments both at the clinic under the guidance of a doctor and at the participant's preferred location.
- Safety follow-up period where participants will have a check-up 28 days after receiving the last dose of RO7276389 and cobimetinib.

**The study will be conducted in 2 parts:**

- Dose escalation where the participants in one group will receive study treatment at a certain dose and once this dose is considered tolerable, the next group of participants will receive a higher dose. A participant's dose will be increased if the doctors think that the treatment is beneficial and decreased if there are side effects. The effect of food on distribution and elimination of the study treatment will also be studied.
- Dose Expansion where a larger group of participants will be included. All participants will get the same dose of study treatment. The dose for Part 2 will be based on the findings from Part 1.

**Participants will be placed in one of the following treatment groups.**

- RO7276389 group: The first few participants, up to 3 in number, will get a single dose of RO7276389, to see how the drug is distributed and then eliminated from the body. After three days, participants will receive the study drug, given as a tablet, every morning by mouth with a full glass of water. The dose for new participants joining the study will be adjusted according to the test results of previous participants. Participants joining the study at later stages will get higher doses of the study drug.
- RO7276389 and cobimetinib group: Participants will get RO7276389 tablets to be taken by mouth once a day for 28 consecutive days (or 1 cycle) along with cobimetinib tablets, also to be taken by mouth once a day for 21 consecutive days. Cobimetinib will not be given from Day 21 to 28 of the treatment cycle.

Participants will continue to take RO7276389 alone or in combination with cobimetinib on a regular basis unless their cancer worsens, they experience severe side effects, or they decide that they no longer want to participate in the study. Treatment may also be stopped earlier than planned if the study doctor feels that the participant is not benefitting from the treatment. After the final dose of study treatment, the study doctor will follow-up participants every 3 months for as long as they agree to it.

**What are the possible benefits and risks of participating?**
Participants will not receive any benefit from participating in this study, but the information that is learned may help people with certain cancers in the future.

Participants may have side effects from the drugs or procedures used in this study that are mild to severe and even life-threatening, and they can vary from person to person. The potential side effects related to the study drug, based on laboratory studies or knowledge of similar drugs, are listed below:

- Skin problems like rash, dry skin, hair loss, and skin cancer
- Diarrhoea or loose stools
- Joint pain
- Kidney problems causing side-effects such as dehydration, urinating less than usual, feeling sick, diarrhoea, confusion, and drowsiness
- Heart problems causing symptoms like dizziness, feeling faint, or palpitations (an irregular heartbeat).

The following are the additional risks associated with cobimetinib (for participants receiving RO7276389 in combination with cobimetinib):

- Increased risk of bleeding. Types of bleeding associated with cobimetinib include nosebleeds, bleeding of the gums, blood in the urine, rectal bleeding, unusual vaginal bleeding, and bleeding within the brain.

- Disturbances in vision caused by swelling and redness of the middle layer of the eye. Other visual changes that can occur are because of the separation of the layers of tissue on the back of the eye that are responsible for sight. This causes symptoms like blurred vision, seeing halos, distorted vision, areas of missing vision, etc.
- Heart problems that can lead to inadequate pumping of the blood
- Serious muscle problem called rhabdomyolysis which may lead to life-threatening complications of chemical imbalances in the blood and kidney injury
- Increase in liver enzymes, which may indicate liver damage or infection
- Swelling in the lungs that can decrease the level of oxygen in the blood

There may be a risk in exposing an unborn child to a study drug, and all risks are not known at this time. Women and men must take precautions to avoid exposing an unborn child to study drugs. If participants are pregnant, become pregnant, or are currently breastfeeding, participants cannot take part in this study.

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

**When is the study starting and how long is it expected to run for?**
September 2021 to March 2024

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

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