ForPatients
by Roche

Glioblastoma

A clinical trial to look at how safe RO7428731 is at different doses, how the body processes it, and what effects RO7428731 has on the body in people with glioblastoma that has the marker EGFRvIII

A Study Evaluating the Safety, Pharmacokinetic and Anti-tumor Activity of RO7428731 in Participants With Glioblastoma

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	6 Countries	NCT05187624 2022-502863-39-00 BP42573

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

An open-label, multicenter, phase I study evaluating the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary clinical activity of RO7428731 in participants with glioblastoma expressing mutant epidermal growth factor receptor variant III (EGFRvIII)

Trial Summary:

This is an open-label, multicenter study to assess safety, tolerability, pharmacokinetics (PK), immunogenicity, pharmacodynamics (PD), and preliminary efficacy of RO7428731 administered as a monotherapy in participants with newly diagnosed or recurrent epidermal growth factor receptor variant III (EGFRvIII)-positive glioblastoma (GBM).

Hoffmann-La Roche	Phase 1
Sponsor	Phase

NCT05187624 2022-502863-39-00 BP42573
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is the BP42573 clinical trial needed?

Glioblastoma is a fast-growing (aggressive) type of brain tumour. Current standard-of-care treatment for glioblastoma includes surgery and radiotherapy with or without chemotherapy. However, the outlook for people is poor and new treatments are needed to improve health outcomes and quality of life for people with glioblastoma. RO7428731 is a drug that helps the body's immune system fight cancer (known as 'immunotherapy'). Up to 1 in 3 people with glioblastoma have tumour cells with a marker called epidermal growth factor receptor variant III (EGFRvIII), which RO7428731 can target. RO7428731 attaches to EGFRvIII on the tumour cells and cells from the immune system. This brings them closer together and activates the immune cell to kill the tumour cell. RO7428731 is an experimental drug, which means health authorities have not approved it for treating glioblastoma. This clinical trial aims to find out whether RO7428731 at different doses has any effects (good or bad), what happens to RO7428731 once it is in the body and what RO7428731 does to the body.

2. How does the BP42573 clinical trial work?

This clinical trial is recruiting people with glioblastoma that has the marker EGFRvIII. People who take part in this clinical trial (participants) will be given the clinical trial treatment RO7428731 for as long as it can help them. Groups of participants will be given increasing doses of RO7428731, depending on when they start the trial and the stage of their cancer. Participants will stay in the hospital for at least 24 hours after being given the first one or two doses of RO7428731 and when being given a higher dose than before. The clinical trial doctor will see them regularly (with more visits over the first 4 months of the trial) and twice over the 2 months after the last dose. These hospital visits will include checks to see how the participant responds to the treatment and any side effects (unwanted effects of a drug or medical treatment) they may have. Total time of participation in the clinical trial could be more than 2 years, depending on how well a participant responds to treatment. Participants can stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the BP42573 clinical trial?

The main clinical trial endpoints (the main results measured in the trial) are the number, type and seriousness of side effects, and the maximum dose of RO7428731 that can be given without unmanageable side effects.

The other clinical trial endpoints include:

- How the body breaks down and processes RO7428731
- The number of participants who make antibodies to RO7428731 and how many they make
- The effect of antibodies to RO7428731 on how the body processes them and the number, type and seriousness of side effects

- The number of participants with a tumour that is smaller or the same size after treatment
- How much time there is between cancer getting better and then getting worse
- The length of time between the start of the trial and participants' cancer getting worse
- How long participants live

4. Who can take part in this clinical trial?

People can take part in this trial if they are at least 18 years old and have completed standard-of-care treatment for glioblastoma. People may not be able to take part in this trial if they are not able to have a magnetic resonance imaging (MRI) scan, have tumours that are in or are close to critical structures in the brain, or have glioblastoma that has come back more than twice or has spread to other parts of the body. People cannot take part if they have certain other medical conditions, such as bleeding/clotting disorders, uncontrolled brain and/or spinal cord diseases, and certain infections, or if they have previously received certain treatments, such as another immunotherapy for glioblastoma. Women who are pregnant or breastfeeding and people who do not agree to prevent pregnancy during and for a certain period after the trial cannot take part. In addition, women cannot donate eggs, and men cannot donate sperm during and for a certain time period after the trial.

5. What treatment will participants be given in this clinical trial?

Everyone who joins this clinical trial will be given RO7428731 as an infusion (into the vein) every 3 weeks for up to 1 year (or longer if the participant benefits from the treatment), or until their cancer gets worse, they have unmanageable side effects or decide to leave the trial. Participants may be given a pre-treatment drug called obinutuzumab in the week before the first dose of RO7428731 to stop the body from making antibodies (which could stop RO7428731 from working properly). If a participant has a side effect to RO7428731 treatment due to an overreaction of the immune system (called 'cytokine release syndrome'), they may be given another drug called tocilizumab. This is an open-label trial, which means everyone involved, including the participant and the clinical trial doctor, will know the clinical trial treatment the participant has been given.

6. Are there any risks or benefits in taking part in this clinical trial?

The safety or effectiveness of the experimental treatment or use may not be fully known at the time of the trial. Most trials involve some risks to the participant. However, it may not be greater than the risks related to routine medical care or the natural progression of the health condition. People who would like to participate will be told about any risks and benefits of taking part in the clinical trial, as well as any additional procedures, tests, or assessments they will be asked to undergo. All of these will be described in an informed consent document (a document that provides people with the information they need to decide if they want to volunteer for the clinical trial).

Risks associated with the clinical trial drugs

Participants may have side effects from the drugs used in this clinical trial. Side effects can be mild to severe, even life-threatening, and vary from person to person. Participants will be closely monitored during the clinical trial and safety assessments will be performed regularly.

RO7428731 has not yet been tested in humans. For this reason, this drug's side effects are not yet known. Participants will be told about the possible side effects of RO7428731 based on laboratory studies or knowledge of similar drugs and known side effects of obinutuzumab and tocilizumab based on prior clinical experience. RO7428731, obinutuzumab and tocilizumab will be given as infusions into the vein (intravenous infusions). Participants will be told about any known side effects of intravenous infusions.

Potential benefits associated with the clinical trial

Participants' health may or may not improve from participation in the clinical trial. Still, the information collected may help other people with similar medical conditions in the future.

Inclusion Criteria:

Inclusion criteria for all participants:

- Life expectancy of greater than or equal to 12 weeks, in the opinion of the Investigator
- Diagnosis of GBM based on World Health Organization (WHO) classification of central nervous system (CNS) tumors, 5th edition
- Participants must have confirmed EGFRvIII-expression
- Karnofsky Performance Status (KPS) Score of >=70%
- Adequate organ functions prior to start of study treatment
- Willingness to abide by contraceptive measures for the duration of the study.

Inclusion criteria for Part I and Part II only:

- Participants whose tumors have an unmethylated (Part I and Part II) or methylated (Part I only) O6-methylguanine-DNA methyltransferase (MGMT) promotor status based on local assessment
- Participants (in Part I): Adult participants with newly diagnosed EGFRvIII-positive GBM with unmethylated MGMT promotor status who have completed standard of care therapy with surgical resection and adjuvant radiotherapy with or without concomitant temozolomide. Participants are allowed to have received any number of cycles of temozolomide maintenance. Adult participants with newly diagnosed EGFRvIII-positive GBM with methylated MGMT promotor status who have completed standard of care with surgical resection and adjuvant radiotherapy with concomitant and maintenance temozolomide or discontinued temozolomide maintenance due to reasons other than progressive disease.
- Participants (in Part II): Adult participants with newly diagnosed EGFRvIII-positive GBM with unmethylated MGMT promotor status who have completed standard of care therapy with surgical resection and adjuvant radiotherapy with or without concomitant temozolomide.

Inclusion criteria for Part III and Part IV A only:

- Documented first or second recurrence of GBM
- At least one measurable GBM lesion as per Response Assessment in Neuro-Oncology (RANO) criteria prior to initiation of study treatment.

Exclusion Criteria:

Exclusion criteria for all participants:

- Participants with infratentorial tumors and tumors primarily located in or close to critical structures (e.g., brain stem)
- Presence of extracranial metastatic or leptomeningeal disease
- Known hypersensitivity to immunoglobulins or to any other component of the investigational medicinal product formulation
- Active bleeding or pathological condition that carries a high risk of bleeding, including inherited and acquired coagulopathies
- Participants unable to undergo an MRI with contrast.

Exclusion criteria for Part I and Part II only:

- Recurrent malignant gliomas
- Any prior anti-tumor treatment for GBM: tumor resection, adjuvant radiotherapy with or without concomitant temozolomide and temozolomide maintenance (Part I only) must be the only tumor-directed treatment that the participant has received for GBM.

Exclusion criteria for Part III and Part IV A only:

- More than two recurrences of GBM
- Prior anti-EGFRvIII-targeting agents (including vaccines), anti-angiogenic therapy, and/or gene therapy for the treatment of GBM and gliomas.