ForPatients
by Roche

Cancer

A Study Evaluating Single-agent Inavolisib and Inavolisib Plus Atezolizumab in PIK3CA-Mutated Cancers

Trial Status	Trial Runs In	Trial Identifier
Recruiting	3 Countries	NCT06496568 2021-006618-36 CO43909

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:

A Phase I/Ib Study Evaluating Single-Agent Inavolisib and Inavolisib Plus Atezolizumab in PIK3CA-Mutated Cancers

Trial Summary:

The purpose of the study is to assess the safety and efficacy of inavolisib as a single-agent and in combination with atezolizumab in participants with phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha isoform (PIK3CA)-mutated cancers, including previously treated head and neck squamous cell carcinoma (HNSCC).

Hoffmann-La Roche	Phase 1
Sponsor	Phase

NCT06496568 2021-006618-36 CO43909
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is this study needed?

Cancer is a health condition where the body's cells start growing and multiplying in an uncontrolled and abnormal way. These cells do not follow the usual pattern of cell division and growth. Instead, they form a lump or mass called a tumour. Head and neck squamous cell carcinoma (HNSCC) is a type of cancer that forms in the head or neck. For some people, the cancer spreads to other parts of the body (known as ‘metastatic’ cancer). Or

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the cancer returns after some time has passed when it could not be detected (known as ‘recurrent’ cancer).

Some cancers have a change in a gene called PIK3CA. A gene is a section of DNA that has instructions for making the body. Cells that have a changed PIK3CA gene are able to survive and grow out of control. They become cancers. Cancers with a change in PIK3CA are called ‘PIK3CA-positive’. Better treatments are needed for PIK3CA-positive cancers that are recurrent or have spread to other parts of the body.

This study is testing a medicine called inavolisib on its own and with another medicine called atezolizumab. They are being developed to treat PIK3CA-positive cancers. Health authorities (like the U.S. Food and Drug Administration and European Medicines Agency) have approved atezolizumab for treating certain cancers. Inavolisib and atezolizumab are experimental medicines in this study. This means health authorities have not approved them for the treatment of PIK3CA-positive cancers or HNSCC.

This study aims to test how safe inavolisib is with or without atezolizumab, and how well they work against PIK3CA-positive cancers. This study will also look at what happens to inavolisib once it is in the body.

2. Who can take part in the study?

People of 18 years of age or older can take part in the study if they have PIK3CA-positive HNSCC that has either spread to other parts of the body, is recurrent, or both. They must have also been treated for HNSCC after the cancer came back or spread.

People may not be able to take part in this study if:

- Their cancer can be treated with surgery and/or radiotherapy
- They have received certain treatments
- They have certain medical conditions, such as infections

People who are pregnant, or currently breastfeeding cannot take part in the study.

3. How does this study work?

Participants will be screened to check if they are able to participate in the study. The screening period will take place from 1 day to 1 month before the start of treatment.

Everyone who joins this study will be put into 1 of 2 groups. This will depend on when the participant joins the study and any other medical conditions they have. It will also depend on what treatments they have been given and if they can be given an intravenous or ‘IV’ infusion (drip into a vein given slowly).

Participants in Group A will be given:

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- Inavolisib as a tablet to be swallowed once a day

Participants in Group B will be given:

- Inavolisib as a tablet to be swallowed once a day
- AND atezolizumab as an IV infusion every 3 weeks

This is an open-label study. This means everyone involved, including the participant and the study doctor, will know the study treatment the participant has been given.

During this study, the study doctor will see participants regularly. They will see how well the treatment is working and any unwanted effects participants may have. Participants will have up to 3 follow-up visits once a month after completing the study treatment, during which the study doctor will check on the participant's well-being. Then, follow-up visits will be every 2 to 3 months until a participant starts another treatment or their cancer gets worse. Total time of participation in the study could be more than 6 months. Participants have the right to stop study treatment and leave the study at any time, if they wish to do so.

4. What are the main results measured in this study?

The main result measured in the study to assess if the medicines have worked is the number and seriousness of unwanted effects.

Other key results measured in the study include:

- How many participants have a specific level of reduction in the size of their tumour that lasts for more than 1 month
- How many participants have a specific level of reduction in the size of their tumour
- How much time there is between the participant's cancer first responding to treatment and the cancer getting worse
- The number of participants whose tumours shrink or stay the same for at least 6 months with study treatment
- How long participants live without their cancer getting worse
- How inavolisib gets to different parts of the body, and how the body changes and gets rid of it

5. Are there any risks or benefits in taking part in this study?

Taking part in the study may or may not make participants feel better. But the information collected in the study can help other people with similar health conditions in the future.

It may not be fully known at the time of the study how safe and how well the study treatment works. The study involves some risks to the participant. But these risks are generally not greater than those related to routine medical care or the natural progression of the health condition. People interested in taking part will be informed about the risks

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and benefits, as well as any additional procedures or tests they may need to undergo. All details of the study will be described in an informed consent document. This includes information about possible effects and other options of treatment.

Risks associated with the study drugs Participants may have unwanted effects of the drugs used in this study. These unwanted effects can be mild to severe, even life-threatening, and vary from person to person. During this study, participants will have regular check-ups to see if there are any unwanted effects.

Inavolisib and atezolizumab Participants will be told about the known unwanted effects of inavolisib and atezolizumab, and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects of inavolisib include a high level of sugar in the blood, frequent watery stools, wanting to throw up, throwing up, rash, the inside linings of the body, like the mouth and nose, get irritated, and inflammation or ulcers of the lip or mouth. Known unwanted effects of atezolizumab include cough, pain or discomfort in the head, back, joints, muscles or bones, frequent watery stools, feeling less hungry than usual and feeling tired or weak. Known unwanted effects of IV infusions include throwing up, wanting to throw up, a feeling of coldness that makes the body shiver, low or high blood pressure, fever, reddening of the skin, pain or discomfort in the head, rapid heart rate, heart beat out of rhythm, frequent, watery stools, shortness of breath and cough.

The study medicine(s) may be harmful to an unborn baby. Women and men must take precautions to avoid exposing an unborn baby to the study treatment.

Inclusion Criteria:

- Histologically or cytologically confirmed recurrent and/or metastatic HNSCC that has been previously treated with systemic therapy in the recurrent and/or metastatic setting
- Documented positive or negative human papillomavirus (HPV) status as determined locally by p16 immunohistochemistry (IHC; preferred), in situ hybridization, and/or by polymerase chain reaction-based assay
- Eligible participants must not be suitable for treatment with surgery and/or radiation
- Confirmation of biomarker eligibility: Valid results from either central testing of blood or local testing of blood or tumour tissue documenting PIK3CA-mutated tumour status
- Consent to provide fresh (preferred) or archival tumour tissue specimen
- Negative hepatitis B surface antigen (HBsAg) and total hepatitis B core antibody (HBcAb) test or positive total HBcAb test followed by a negative hepatitis B virus (HBV) DNA at screening
- Negative hepatitis C virus (HCV) antibody test at screening, or positive HCV antibody test followed by a negative HCV RNA test at screening
- Measurable disease per RECIST v1.1
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1
- Life expectancy of >=12 weeks

Exclusion Criteria:

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- Prior treatment with any phosphatidylinositol 3-kinase (PI3K), protein kinase B (AKT), or mammalian target of rapamycin (mTOR) inhibitor, or any agent whose mechanism of action is to inhibit the PI3K/AKT/mTOR pathway
- Appropriate for treatment with surgery and/or radiation at the time of entry into the study, as per national or local treatment guidelines
- Type II diabetes requiring ongoing systemic treatment at the time of study entry; or any history of Type I diabetes
- Malabsorption syndrome or other condition that would interfere with enteral absorption
- Known and untreated, or active central nervous system (CNS) metastases (progressing or requiring anticonvulsants or corticosteroids for symptomatic control). Participants with a history of treated CNS metastases are eligible provided they meet specified criteria
- Uncontrolled pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures twice per week or more frequently
- Serious infection requiring IV antibiotics within 7 days prior to Day 1 of Cycle 1
- Treatment with a live, attenuated vaccine within 4 weeks prior to initiation of study treatment, or anticipation of the need for such a vaccine during study treatment
- Any concurrent ocular or intraocular condition (e.g., cataract or diabetic retinopathy) that, in the opinion of the investigator, would require medical or surgical intervention during the study period to prevent or treat vision loss that might result from that condition
- Active inflammatory (e.g., uveitis or vitritis) or infectious (e.g., conjunctivitis, keratitis, scleritis, or endophthalmitis) conditions in either eye or history of idiopathic or autoimmune-associated uveitis in either eye
- Requirement for daily supplemental oxygen
- Symptomatic active lung disease, including pneumonitis
- History of or active inflammatory bowel disease (e.g., Crohn's disease or ulcerative colitis) or any active bowel inflammation (including diverticulitis)
- Known Human Immunodeficiency Virus (HIV) infection
- Current severe, uncontrolled systemic disease (e.g., clinically significant cardiovascular, pulmonary, metabolic, or infectious disease) or any other diseases, active or uncontrolled pulmonary dysfunction, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug, that may affect the interpretation of the results, or that renders the participant at high risk from treatment complications
- Chemotherapy, radiotherapy, or any other anti-cancer therapy within 2 weeks before enrolment
- Investigational drug(s) within 4 weeks before enrolment
- Unresolved toxicity from prior therapy, except for hot flashes, alopecia, and Grade <=2 peripheral neuropathy
- History of other malignancy within 5 years prior to screening, with specified exceptions
- History of or active clinically significant cardiovascular dysfunction
- Any serious medical condition or abnormality in clinical laboratory tests that, in the investigator's judgment, precludes the participant's safe participation in and completion of the study)
- Chronic corticosteroid therapy of >=10 mg of prednisone per day or an equivalent dose of other anti-inflammatory corticosteroids or immunosuppressants for a chronic disease
- Allergy or hypersensitivity to components of the inavolisib formulation
- Treatment with strong CYP3A4 inducers or strong CYP3A4 inhibitors within 1 week or five drug-elimination half-lives, whichever is longer, prior to initiation of study treatment
- Major surgical procedure, or significant traumatic injury, within 28 days prior to Day 1 of Cycle 1; or anticipation of the need for major surgery during study treatment
- Minor surgical procedures <7 days prior to the first dose of study treatment

Exclusion criteria specific to arms utilizing atezolizumab:

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- Prior serious immune-mediated toxicities resulting from treatment with any checkpoint inhibitor including, but not limited to, atezolizumab, pembrolizumab, or nivolumab
- Treatment with any checkpoint inhibitor within 5 half-lives of Day 1 of Cycle 1
- Uncontrolled or symptomatic hypercalcemia
- Active or history of autoimmune disease or immune deficiency, including, but not limited to, myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, antiphospholipid antibody syndrome, Wegener granulomatosis, Sjögren syndrome, Guillain-Barré syndrome, or multiple sclerosis, with specified exceptions
- History of idiopathic pulmonary fibrosis, organizing pneumonia (e.g., bronchiolitis obliterans), drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest CT scan; a history of radiation pneumonitis in the radiation field (fibrosis) is permitted
- Active tuberculosis
- Severe infection within 4 weeks prior to initiation of study treatment, including, but not limited to, hospitalization for complications of infection, bacteraemia, or severe pneumonia
- Treatment with therapeutic oral or IV antibiotics within 2 weeks prior to initiation of study treatment; participants receiving prophylactic antibiotics may be eligible for the study
- Prior allogeneic stem cell or solid organ transplantation
- Current treatment with anti-viral therapy for HBV
- Treatment with systemic immunostimulatory agents within 4 weeks or five drug-elimination half-lives of the drug (whichever is longer)
- Treatment with systemic immunosuppressive medication within 2 weeks prior to initiation of study treatment, or anticipation of the need for systemic immunosuppressive medication during study treatment, with specified exceptions
- Poor peripheral venous access that would preclude repeated IV infusions
- History of severe allergic anaphylactic reactions to chimeric or humanized antibodies or fusion proteins
- Known hypersensitivity to Chinese hamster ovary cell products or to any component of the atezolizumab formulation

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