ForPatients
by Roche

Metastatic MelanomaMalignant Melanoma

A clinical trial to look at how safe RO6874281 is in combination with another drug called pembrolizumab, and to look at how well the combination works to treat melanoma.

A Phase IB Study To Evaluate Safety And Therapeutic Activity Of RO6874281, An Immunocytokine, Consisting Of Interleukin-2 Variant Targeting Fibroblast Activation Protein-#, In Combination With Pembrolizumab (Anti-Pd-1), In Participants With Previously Untreated Advanced And/Or Metastatic Melanoma

Trial Status	Trial Runs In	Trial Identifier
Completed	7 Countries	NCT03875079 2018-003872-11 BP41054

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 Ib Study to Evaluate Safety and Therapeutic Activity of RO6874281, an Immunocytokine, Consisting of Interleukin-2 Variant (IL-2v) Targeting Fibroblast Activation Protein-Α (FAP), in Combination with Pembrolizumab (Anti-PD-1), in Participants with Advanced or Metastatic Melanoma

Trial Summary:

This is an open-label, multicenter, Phase Ib study to evaluate the safety and therapeutic activity of RO6874281 in combination with pembrolizumab. The study will consist of 3 parts: a safety run-in (Part I: Cohorts 1.1. and 1.2) and two expansion parts (Parts II and III). Part II will start once all participants in Cohort 1.1 have completed the observation period. Part III will start once all participants in Cohorts 1.1 and 1.2 have completed the observation period.

Hoffmann-La Roche
Sponsor

Phase 1
Phase

NCT03875079 2018-003872-11 BP41054
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers

All	#18 Years	No

How does the BP41054 clinical trial work?
This clinical trial is recruiting people who have a type of skin cancer called melanoma that has spread to other parts of the body and cannot be removed by surgery.

The purpose of this clinical trial is to find out what effects, good or bad, RO6874281 plus pembrolizumab has on patients with advanced and/or metastatic melanoma. By giving the two drugs together it is hoped that the effects will be better than giving the drugs on their own.

The clinical trial will be done in three parts:

- The aim of Part 1 is to confirm:
    - how safe RO6874281 is in combination with pembrolizumab
    - how well patients can cope with any side effects
    - the dose that will be used in Parts 2 and 3 of the study.
- The aim of Parts 2 and 3 is to find out:
    - how safe RO6874281 is in combination with pembrolizumab
    - how well patients can cope with any side effects
    - the most effective way to give the study drugs.

If you take part in this clinical trial, you will receive a combination of RO6874281 and pembrolizumab. The exact course of treatment you receive will depend on which part of the study you join and whether you have received any previous treatment with a type of drug known as a ‘checkpoint inhibitor’ (pembrolizumab is an example of this type of drug).

How do I take part in this clinical trial?
To be able to take part in this clinical trial, you must have melanoma that has spread to other parts of your body and be at least 18 years old.

You must not have:

- a tumour that is getting worse quickly or is causing complications to your vital organs, such as breathing difficulties
- cancer that has newly spread to the brain or spinal cord – however, if your cancer has previously spread to the brain and been successfully treated you may be able to join the trial
- a history of treated cancer that spread to the brain or spinal cord without causing any symptoms.

You will be put into 1 of 2 groups based on whether or not you have received previous treatment with a checkpoint inhibitor:

Group 1

Everyone in this group must have either:

- not yet received any treatment, OR
- tested positive for a certain genetic mutation called ‘BRAF’ and received previous treatment with a drug targeting BRAF that was not successful.

Group 2

Everyone in this group must have:

- received previous treatment for melanoma with a checkpoint inhibitor, to which your disease did not respond or initially responded and then stopped.

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor. If your doctor thinks that you might be able to take part in this clinical trial, he/she may refer you to the closest clinical trial doctor. They will give you all the information you need to make your decision about taking part in the clinical trial. You can also find the clinical trial locations on this page.

You will have some further tests to make sure you will be able to take the treatments given in this clinical trial. Some of these tests or procedures may be part of your regular medical care. They may be done even if you do not take part in the clinical trial. If you have had some of the tests recently, they may not need to be done again.

Before starting the clinical trial, you will be told about any risks and benefits of taking part in the trial. You will also be told what other treatments are available so that you may decide if you still want to take part.

While taking part in the clinical trial, both men and women (if you are not currently pregnant but can become pregnant) will need to either not have heterosexual intercourse or take contraceptive medication for safety reasons.

What treatment will I be given if I join this clinical trial?
Everyone who joins this clinical trial will be given both RO6874281 and pembrolizumab, given as infusions into your vein. The exact treatment schedule will depend on which part of the study you join (Part 1 will run before Parts 2 and 3) and which group you are put into based on your previous treatment. If you join Part 1 you will not be able to join Parts 2 or 3.

Part 1 (up to 2 years)

Group 1 will be given RO6874281 and pembrolizumab every 3 weeks.

Group 2 will be split into two groups randomly (like flipping a coin) and given either:

- RO6874281 and pembrolizumab every 3 weeks, OR
- RO6874281 once a week for 3 weeks then every 3 weeks after that, plus pembrolizumab every 3 weeks.

After six patients in each group in Part 1 have completed two dose cycles (6 weeks), researchers will analyse the safety of the dose and decide which dose and schedule should be used in Parts 2 and 3.

Part 2 (up to 2 years)

Group 1 will be given RO6874281 and pembrolizumab every 3 weeks.

Part 3 (up to 2 years)

Group 2 will be split into two groups randomly (like flipping a coin) and given either:

- RO6874281 and pembrolizumab every 3 weeks, OR
- RO6874281 once a week for 3 weeks then every 3 weeks after that, plus pembrolizumab every 3 weeks.

How often will I be seen in follow-up appointments and for how long?
You will be given the clinical trial treatment for as long as it can help you, up to a maximum of 2 years. You are free to stop this treatment at any time. While being given treatment, you will be seen regularly by the clinical trial doctor. These hospital visits will include checks to see how you are responding to the treatment and any side effects that you may be having. After being given your last dose, you will be seen by the clinical trial doctor after about 1 month and again after 3 months.

Inclusion Criteria:

- Histologically confirmed unresectable stage III or stage IV cutaneous or mucosal melanoma (AJCC v8.0).
- Participants need to have known BRAF status.
- CPI naïve melanoma population: Participants with unresectable stage III or stage IV cutaneous or mucosal melanoma who have not received prior treatment for advanced disease. BRAF mutation-positive patients are eligible without prior treatment or after failure of BRAF directed inhibitor therapy.
- CPI experienced melanoma population: Participants with unresectable stage III or stage IV cutaneous melanoma. Participants must have progressed during or after treatment with anti PD-1 antibody therapy, either as monotherapy or in combination with other agent(s).
- Participants should have adequate cardiovascular, hematological, liver, and renal function.
- Participants with unilateral pleural effusion are eligible if they fulfill both of the following: NYHA Class 1; Forced expiratory volume 1 (FEV1) >70% and forced vital capacity (FVC) >70% of predicted value; participants with lung metastases should present with DLCO >60% of predicted value.

Exclusion Criteria:

Medical Conditions

- Rapid disease progression or suspected hyperprogression (as determined by the Investigator) or threat to vital organs or critical anatomical sites requiring urgent alternative medical intervention.
- Known active CNS metastases and/or carcinomatous meningitis/leptomeningeal disease:

Participants with previously treated brain metastases may participate.

- History of treated asymptomatic CNS metastases.
- An active second malignancy (exceptions are non-melanoma skin cancer, cervical carcinoma in situ, or prostate carcinoma that is in remission under androgen deprivation therapy for # 2 years, or participants who have a history of malignancy and have been treated with curative intent and the participant is expected to be cured as per Investigator's assessment).
- Evidence of significant, uncontrolled concomitant diseases that could affect compliance with the protocol or interpretation of results, and known autoimmune diseases or other disease with ongoing fibrosis (such as scleroderma, pulmonary fibrosis. and emphysema).
- Episode of significant cardiovascular/cerebrovascular acute disease within 6 months before study treatment administration.
- Active or uncontrolled infections, including latent tuberculosis.
- Known HIV infection.
- Active hepatitis B virus (HBV) or hepatitis C virus (HCV) infection.
- Severe infection within 4 weeks before study treatment administration, including, but not limited to, hospitalization for complications of infection, bacteremia, or severe pneumonia.
- History of chronic liver disease or evidence of hepatic cirrhosis.
- Dementia or altered mental status that would prohibit informed consent.
- History of autoimmune disease.
- Adverse events related to any previous radiotherapy, chemotherapy, targeted therapy, CPI therapy or surgical procedure that have not resolved to Grade =< 1, except alopecia (any grade) and Grade 2 peripheral neuropathy.
- History of idiopathic pulmonary fibrosis, pneumonitis (including drug induced), organizing pneumonia (i.e., bronchiolitis obliterans, cryptogenic organizing pneumonia, etc.), or evidence of active pneumonitis on screening chest computed tomography (CT) scan.
- Bilateral pleural effusion.
- Severe dyspnea at rest or requiring supplementary oxygen therapy.
- Concurrent therapy with any other investigational drug (defined as a treatment for which there is currently no regulatory authority approved indication).
- Immunomodulating agents: Last dose with any of the following agents, for example, etanercept, infliximab, tacrolimus, cyclosporine, mycophenolic acid, alefacept, or efalizumab (or similar agents) < 28 days before study treatment administration. Regular immunosuppressive therapy (i.e., for organ transplantation, chronic rheumatologic disease)
- Treatment with systemic immunosuppressive medications including, but not limited to prednisone, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-TNF agents within 2 weeks prior to Cycle 1 Day 1.
- Radiotherapy within the last 4 weeks before start of study treatment administration, with the exception of limited field palliative radiotherapy.
- Administration of a live, attenuated vaccine within 4 weeks before Cycle 1 Day 1.
- Major surgery or significant traumatic injury < 28 days before study treatment administration (excluding fine needle biopsies) or anticipation of the need for major surgery during study treatment.
- Known hypersensitivity to any of the components of the RO6874281 drug product or pembrolizumab drug product, including but not limited to hypersensitivity to Chinese Hamster Ovary cell products or other recombinant human or humanized antibodies.
- No prior cytotoxic therapy for unresectable stage III or stage IV disease is permitted.
- Toxicity from prior anti-PD-1 antibody therapy (including adjuvant treatment).