ForPatients
by Roche

Breast Cancer

A clinical trial to look at how safe RO6874281 is, either on its own or in combination with trastuzumab or cetuximab, in patients with different types of solid tumours (BP29842)

A Study Evaluating Safety, Pharmacokinetics, and Therapeutic Activity of RO6874281 as a Single Agent (Part A) or in Combination With Trastuzumab or Cetuximab (Part B or C)

Trial Status	Trial Runs In	Trial Identifier
Completed	9 Countries	NCT02627274 2015-002251-97 BP29842

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, Dose-Escalation, Phase Ia/Ib Study to Evaluate Safety, Pharmacokinetics, and Therapeutic Activity of RO6874281, an Immunocytokine Consisting of Interleukin 2 Variant (IL-2v) Targeting Fibroblast Activation Protein-# (FAP), as a Single Agent (Part A) or in Combination With Trastuzumab or Cetuximab (Part B or C)

Trial Summary:

This first-in-human, open-label, multicenter, Phase Ia/Ib, adaptive, multiple ascending-dose study will evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and preliminary anti-tumor activity of RO6874281 as a single agent (Part A) or in combination with trastuzumab or cetuximab (Part B or C).

Hoffmann-La Roche Sponsor	**Phase 1** Phase

NCT02627274 2015-002251-97 BP29842
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	# 18 Years	No

How does the BP29842 clinical trial work?

The first two parts of this trial to test RO6874281 either on its own or in combination with trastuzumab in people with solid tumours or breast cancer are no longer recruiting patients.

The third part of the clinical trial is still recruiting people who have head and neck cancer, that has either advanced or spread to other parts of the body.

The purpose of this part of the clinical trial is to test the safety of RO6874281 in combination with cetuximab, at different doses and to understand the way the body processes RO6874281.

How do I take part in this clinical trial?

Everyone who joins this part of the trial must have a type of head and neck cancer called ‘squamous cell carcinoma’. The cancer must be inoperable, or have spread to other parts of the body, or have previously gone away after treatment but has now come back.

You must not have cancer that is quickly getting worse or cancer that has spread to the brain or spinal cord that is untreated or causing symptoms.

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? You will receive RO6874281 every week (the dose will depend on the stage of the study when you enrol) and standard doses of cetuximab every week.

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. You are free to stop this treatment at any time. While being given treatment, you will be seen regularly by the clinical trial doctors. 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 treatment, you will be seen by the clinical trial doctor after 1 month and then contacted every 3 months after that.

What happens if I am unable to take part in this clinical trial?
If this clinical trial is not suitable for you, you will not be able to take part. Your doctor will suggest other clinical trials that you may be able to take part in or other treatments that you can be given. You will not lose access to any of your regular care.

For more information about this clinical trial see the **For Expert** tab on the specific ForPatient page or follow this link to ClinicalTrials.gov

Trial-identifier: NCT02627274

Inclusion Criteria:

- Radiologically measurable and clinically evaluable disease
- Absence of rapid disease progression or threat to vital organs or critical anatomical sites requiring urgent alternative medical intervention
- Confirmed at least one tumor lesion with location accessible to safely biopsy per clinical judgment (special requirements apply for Part C; Participants with only one target lesion and no non-target lesions can enroll after documented agreement with the Medical Monitor).
- Life expectancy of greater than or equal to (>=12) weeks
- Eastern Cooperative Oncology Group (ECOG) Performance Status 0-1
- Participants with unilateral pleural effusion (other than non-small cell lung cancer [NSCLC] indication) should fulfill the following criteria for pulmonary and cardiac functions: Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification 0 - 1 level and New York Heart Association (NYHA) classification class 1 or better
- 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
- Adequate cardiovascular, hematological, liver and renal function
- All acute toxic effects of any prior radiotherapy, chemotherapy, or surgical procedure must have resolved to grade less than or equal to (<=) 1, except alopecia (any grade) and Grade 2 peripheral neuropathy
- Negative serum pregnancy test within 7 days prior to study treatment in premenopausal women and women less than (<) 12 months after menopause
- For women who are not postmenopausal and have not undergone surgical sterilization: agreement to remain abstinent or use two adequate non-hormonal methods of contraception, including at least one method with a failure rate of <1 percent (%) per year, during the treatment period and for a period of time after the last dose of study drug(s) as defined in the protocol
- For men: agreement to remain abstinent or use contraceptive measures and agreement to refrain from donating sperm during the treatment period and for at least for at least 2 months after the last dose of study treatment
- For Part A exclusively (RO6874281 monotherapy), confirmed advanced and/or metastatic solid tumor, with at least one tumor lesion of location accessible to biopsy per clinical judgment of the treating

physician, and confirmed progression at baseline; for whom no standard therapy that would confer clinical benefit to the participant exists
- For Part B exclusively (RO6874281 in combination with trastuzumab), participants with metastatic or recurrent or locally advanced human epidermal growth factor receptor 2 (HER2)-positive breast cancer, as defined by the College of American Pathologists HER2 testing guidelines, who have progressed on at least two lines of HER2-directed therapies in the metastatic setting and the last therapy prior to going on study has to contain a HER2-directed antibody; baseline left ventricular ejection fraction (LVEF) of >=50% (measured by echocardiography) predose on Cycle 1 Day 1
- For Part C exclusively (RO6874281 in combination with cetuximab), participants with recurrent, unresectable or metastatic squamous cell carcinoma of the head and neck. Participants can have had standard or experimental treatment, including but not limited to radiation therapy, chemotherapy, or immunotherapy
- Participants with Gilbert's syndrome will be eligible for the study

Exclusion Criteria:

- History of, active, or suspicion of autoimmune disease (exceptions apply)
- Adverse events from prior anti-cancer therapy that have not resolved to Grade 1, except for alopecia, vitiligo, or endocrinopathies managed with replacement therapy
- Symptomatic or untreated central nervous system (CNS) metastases
- History of treated asymptomatic CNS metastases with any of the following: Metastases to the brain stem, midbrain, pons, medulla, cerebellum, or within 10 millimeters (mm) of the optic nerves and chiasm; history of intracranial or spinal cord hemorrhage; lacking radiographic demonstration of improvement upon the completion of CNS-directed therapy and evidence of progression between completion of therapy and the baseline radiographic study; ongoing requirement for dexamethasone; stereotactic or whole brain radiation within 28 days before the start of study treatment; last CNS radiographic study less than 4 weeks since completion of radiotherapy and less than 2 weeks since the discontinuation of corticosteroids; CNS metastases treated by resection or brain biopsy performed within 28 days before the start of study treatment
- Participants with an active second malignancy
- Evidence of significant, uncontrolled concomitant diseases that could affect compliance with the protocol or interpretation of results, including diabetes mellitus, history of relevant pulmonary disorders, and known autoimmune diseases or other disease with ongoing fibrosis
- Participants (all indications) with confirmed bilateral pleural effusion and NSCLC participants with confirmed uni- or bilateral pleural effusion by X-ray are not eligible
- Significant cardiovascular/cerebrovascular disease within 6 months prior to Day 1 of study drug administration
- Active or uncontrolled infections
- Known human immunodeficiency virus (HIV) or known active hepatitis B virus or hepatitis C virus infection
- History of chronic liver disease or evidence of hepatic cirrhosis
- Any other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding that give reasonable suspicion of a disease or condition that would contraindicate the use of an investigational drug
- Major surgery or significant traumatic injury <28 days prior to the first RO6874281 infusion (excluding biopsies) or anticipation of the need for major surgery during study treatment
- Dementia or altered mental status that would prohibit informed consent
- Pregnant or breastfeeding women
- Known hypersensitivity to any of the components of RO6874281
- Concurrent therapy with any other investigational drug
- Immune-related endocrinopathies
- Immunomodulating agents <28 days prior to first dose of study drug

- Treatment with systemic immunosuppressive medications
- Severe dyspnea at rest due to complications of advanced malignancy or requiring supplementary oxygen therapy
- For Part B exclusively, known hypersensitivity to any of the components of trastuzumab
- For Part C exclusively, known hypersensitivity to any of the components of cetuximab
- For Parts A, B, and C, eligibility of participants who require blood transfusion before and after the start of the study treatment should be discussed by the Sponsor and investigator
- For Parts B and C, Participant eligibility for treatment with trastuzumab or cetuximab should be verified against trastuzumab or cetuximab labeling documents.