Protocol RO6874281

An open-label, multicentre, phase II study to evaluate the therapeutic activity of RO6874281, an immunocytokine, consisting of interleukin-2 variant (IL-2V) targeting fibroblast activation protein-A (FAP), in combination with atezolizumab (anti-PD-L1), administered intravenously, in participants with advanced and/or metastatic sold tumors.

This is the trial summary as assessed on clinicaltrials.gov on 27/11/2018

Minor changes in the protocol may occur. You can check this on this direct link:

https://clinicaltrials.gov/ct2/show/NCT03386721?term=BP40234&rank=1

Trial Design :

This is an open-label, multicenter, Phase II study to evaluate the antitumor activity of RO6874281 in combination with atezolizumab in participants with advanced and/or metastatic solid tumors.

Inclusion Criteria:

Participants who have progressed on at least one previous regimen of anticancer therapy (chemotherapy, mutation targeted therapy, and/or CPI therapy)

Measurable disease, as defined by RECIST Version 1.1

Eastern Cooperative Oncology Group (ECOG) Performance Status 0 or 1 or Karnofsky Performance Score greater than or equal to (>=) 70

Life expectancy of >=12 weeks

Confirmed at least one tumor lesion with location accessible to safely biopsy per clinical judgment of the treating physician (not applicable to Part 1 Cohort A)

Consent to provide an archival tumor tissue sample (if available, applicable to all participants)

Willingness to undergo baseline and on-treatment tumor biopsies for pharmacodynamics (PD) biomarker analysis (not applicable to Part 1 Cohort A)

Adequate cardiovascular function as defined in the study protocol

AEs related to any previous 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

Adequate haematological, liver, and renal functions.

Participants with unilateral pleural effusion (indications other than NSCLC) are eligible if they fulfill both of the following: (a) New York Heart Association (NYHA) Class 1; (b) Global initiative for obstructive lung disease test level 1 (forced expiratory volume 1 / forced vital capacity less than [<] 0.7 and forced expiratory volume >=80 percent [%] predicted) (use of bronchodilators allowed)

Participants with Gilbert's syndrome will be eligible for the study

CPI-Naïve Participants (Part 1 Cohort A + C):

Participants must not have received CPI therapy (for example, anti- cytotoxic T-lymphocyte-associated protein 4 [anti-CTLA-4], anti-programmed death-1 [anti-PD-1]/ anti-PD-L1) before study enrollment

Participant must have progressed on at least one previous systemic therapy for advanced or metastatic disease

Participants may be enrolled if they are ineligible for standard of care (SoC) therapy or if they are not willing to receive conventional therapy

Participants whose tumors have a known sensitizing mutation (for example, Epidermal growth factor receptor [EGFR], Anaplastic Lymphoma Kinase [ALK] etc.) must have experienced disease progression (during or after treatment) or intolerance to treatment with a respective targeted therapy

CPI-Experienced Participants (Part 1 Cohort B and Part III Cohort H):

Participants must have experienced documented disease progression on or after CPI therapy (investigational or approved)

The CPI may have been administered as monotherapy or as part of a combination regimen at any time during the anti-cancer treatment before study enrollment

Participants with suspected or documented disease progression within the first 12 weeks of CPI therapy may not be eligible and require discussion with the Sponsor. Screening tumor assessment should confirm previous progression

No history of severe immune-related adverse effects from CPI treatment (National Cancer Institute Common Terminology Criteria for AEs [NCI CTCAE] Grade 3 and 4)

CPI-Experienced Participants (Part 1 Cohort D):

Participants who experienced disease progression during or following treatment with a platinum-containing regimen and a checkpoint inhibitor, given in combination as one line of therapy or as two separate lines of therapy.

Participants should have experienced disease progression on docetaxel therapy.

Participants with High-Tumor PD-L1 Expression (Part 2 Cohort E)

Participants with a PD-L1 TPS greater than 50%, who have not received any prior systemic therapy for metastatic NSCLC and who must not have any target mutations and/or rearrangements.

CPI-Experienced Participants (Part 1 Cohort F):

CPI-Experienced, docetaxel naive participants (NSCLC) who experienced disease progression during or following treatment with a platinum - containing regimen. Participants will receive combination of RO6874281 and atezolizumab in a Q3W schedule.

Exclusion Criteria:

Symptomatic or untreated central nervous system (CNS) metastases

History of treated asymptomatic CNS metastases as described in the protocol

Spinal cord compression not definitively treated with surgery and/or radiation or previously diagnosed and treated spinal cord compression without evidence that disease has been clinically stable for >=2 weeks before enrollment

Leptomeningeal disease

An active second malignancy

Penetrating tumor infiltration

Evidence of significant, uncontrolled concomitant diseases that could affect compliance with the protocol or interpretation of results

Episode of significant cardiovascular/cerebrovascular acute disease within 6 months before study treatment administration

History of significant vascular disease (for example, aortic aneurysm, aortic dissection)

Peripheral arterial thrombosis within 6 months before study treatment administration

Active or uncontrolled infections

Human immunodeficiency virus (HIV) or hepatitis B or hepatitis C virus infection

Known active bacterial, viral, fungal, mycobacterial, parasitic, or other infection (excluding fungal infections of nail beds) or any major episode of infection requiring treatment with IV antibiotics or hospitalization within 4 weeks before study treatment administration

History of chronic liver disease or evidence of hepatic cirrhosis

Serious, non-healing wound; active ulcer; or untreated bone fracture

Dementia or altered mental status that would prohibit informed consent

History of, active or suspicion of autoimmune disease

History of idiopathic pulmonary fibrosis, pneumonitis (including drug-induced), organizing pneumonia (bronchiolitis obliterans, cryptogenic organizing pneumonia, etc.), or evidence of active pneumonitis on screening chest computed tomography (CT) scan. History of radiation pneumonitis in the radiation field (fibrosis) is permitted

Bilateral pleural effusion confirmed by X-ray

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

Concurrent therapy with any other investigational drug

Immunomodulating agents as described in study protocol

Chronic use of steroids

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 or at any time during the study and 5 months after the last dose of atezolizumab

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 atezolizumab drug product

Severe dyspnea at rest or requiring supplementary oxygen therapy

CPI-Naïve Participants Only (Part 1 Cohort A & C):

- Previous CPI therapy (for example, anti-CTLA-4, anti-PD-1/L1)

CPI-Experienced Participants Only (Part 1 Cohort B + D):

Participants who discontinued CPI therapy for CPI-associated toxicity or intolerability

Any history of an immune-related Grade >=3 AE attributed to previous cancer immunotherapy (with the exception of endocrinopathy managed with replacement therapy)

CPI-Experienced Participants Only (Part 1 Cohort D):

- Known sensitivity and contraindications to the comparative chemotherapy agent gemcitabine or vinorelbine.

Participants in Part II

- Participants with pleural effusion confirmed at screening by x-ray.