ForPatients
by Roche

Non-Small Cell Lung Cancer (NSCLC)Triple Negative Breast CancerBladder CancerColorectal Cancer (CRC)Malignant MelanomaRenal Cell Cancer (RCC)Non Small Cell Lung CarcinomaMelanomaHead and Neck Cancer

A Study of RO7198457 (Personalized Cancer Vaccine [PCV]) as a Single Agent and in Combination With Atezolizumab in Participants With Locally Advanced or Metastatic Tumors

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	8 Countries	NCT03289962 2017-001475-23 GO39733

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 1a/1b Open-Label, Dose-Escalation Study of the Safety and Pharmacokinetics of RO7198457 as a Single Agent and in Combination With Atezolizumab in Patients With Locally Advanced or Metastatic Tumors

Trial Summary:

This is a Phase 1a/1b, open-label, multicenter, global, dose-escalation study designed to evaluate the safety, tolerability, immune response, and pharmacokinetics of autogene cevumeran (RO7198457) as a single agent and in combination with atezolizumab (MPDL3280A, an engineered anti-programmed death-ligand 1 [anti-PD-L1] antibody).

Genentech, Inc. Sponsor	**Phase 1** Phase

NCT03289962 2017-001475-23 GO39733
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	# 18 Years	No

Inclusion Criteria:

- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1

- Life expectancy greater than or equal to (>=12 weeks)
- Adequate hematologic and end-organ function
- Measured or calculated creatinine clearance >=50 milliliters per minute (mL/min) on the basis of the Cockcroft-Gault glomerular filtration rate estimation

Cancer-Specific Inclusion Criteria:

- Participants with histologic documentation of locally advanced, recurrent, or metastatic incurable malignancy that has progressed after at least one available standard therapy; or for whom standard therapy has proven to be ineffective or intolerable, or is considered inappropriate; or for whom a clinical trial of an investigational agent is a recognized standard of care
- Participants with confirmed availability of representative tumor specimens in formalin-fixed, paraffin-embedded (FFPE) blocks (preferred), or sectioned tissue
- Participants with measurable disease per RECIST v1.1

Additional Inclusion Criteria for Participants in Each Indication-Specific Exploration/ Expansion Cohort of Phase 1b:

- NSCLC Cohorts (CIT-Naive): Participants with histologically confirmed incurable, advanced NSCLC not previously treated with anti-PD-L1/PD-1 and/or with anti-CTLA-4 (investigational or approved), for whom a clinical trial of an investigational agent in combination with an anti-PD-L1/PD-1 antibody is considered an acceptable treatment option (if CIT [including anti-PD-L1/PD-1 agents] is approved as treatment for NSCLC by local regulatory authorities).
- NSCLC Cohort (CIT-Treated): Participants with histologically confirmed incurable, advanced NSCLC previously treated with anti-PD-L1/PD-1 with or without anti-CTLA-4 (investigational or approved)
- Triple negative breast cancer (TNBC) Cohort (CIT-Naive): Participants with histologically confirmed incurable, advanced estrogen receptor (ER)-negative, progesterone receptor-negative, and human epidermal growth factor receptor 2 (HER2)-negative adenocarcinoma of the breast (triple-negative) not previously treated with anti-PD-L1/PD-1 and/or anti-CTLA-4 (investigational or approved)
- Colorectal cancer (CRC) Cohort (CIT-Naive): Participants with histologically confirmed incurable, advanced adenocarcinoma of the colon or rectum not previously treated with anti-PD-L1/PD-1 and/or anti-CTLA-4 (investigational or approved)
- Head and neck squamous cell carcinoma (HNSCC) Cohort (CIT-Naive): Participants with histologically confirmed inoperable, locally advanced or metastatic, recurrent, or persistent HNSCC (oral cavity, oropharynx, hypopharnyx, or larynx) not amenable to curative therapy not previously treated with anti-PD-L1/PD-1 and/or anti-CTLA-4 (investigational or approved)
- Urothelial carcinoma (UC) Cohort (CIT-Naive): Participants with histologically confirmed incurable, advanced transitional cell carcinoma of the urothelium including renal pelvis, ureters, urinary bladder, and urethra, not previously treated with anti-PD-L1/PD-1 with or without anti-CTLA-4 (investigational or approved), for whom a clinical trial of an investigational agent in combination with an anti-PD-L1 antibody is considered an acceptable treatment option, if CIT (including anti-PD-L1/PD-1 agents) is approved as treatment for UC by local regulatory authorities
- UC Cohort (CIT-Treated): Participants with histologically confirmed incurable advanced transitional cell carcinoma of the urothelium (including renal pelvis, ureters, urinary bladder, and urethra) previously treated with anti-PD-L1/PD-1 with or without anti-CTLA-4 (investigational or approved)
- Renal cell carcinoma (RCC) Cohort (CIT-Naive): Participants with histologically confirmed incurable, advanced RCC with component of clear cell histology and/or component of sarcomatoid histology not previously treated with anti-PD-L1/PD-1 and/or anti-CTLA-4 (investigational or approved)
- Melanoma Cohort (CIT-Naive in metastatic setting): Participants with histologically confirmed incurable, advanced melanoma not previously treated with anti-PD-L1/PD-1 and/or anti-CTLA-4 (investigational or approved) in the metastatic setting

- Melanoma Cohort (CIT-Treated): Participants with histologically confirmed incurable, advanced melanoma previously treated with anti-PD-L1/ or PD-1 with or without CTLA-4 (investigational or approved)

Additional Inclusion Criteria for Participants in the Serial-Biopsy Expansion Cohort of Phase 1b:

- Participants must have one of the locally advanced or metastatic solid tumor types specified in the protocol.
- Participants must have accessible lesion(s) that permit a total of two to three biopsies (pretreatment and on-treatment) or one biopsy (on-treatment, if archival tissue can be submitted in place of a pre-treatment biopsy) without unacceptable risk of a significant procedural complication. RECIST lesions should not be biopsied.

Exclusion Criteria:

- Known clinically significant liver disease, including active viral, alcoholic, or other hepatitis, cirrhosis, and inherited liver disease or current alcohol abuse
- Major surgical procedure within 28 days prior to Cycle 1, Day 1, or anticipation of need for a major surgical procedure during the course of the study
- Any other diseases, metabolic dysfunction, physical examination finding, and/or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or that may affect the interpretation of the results or may render the participant at high risk from treatment complications
- Previous splenectomy
- Known primary immunodeficiencies, either cellular (e.g., DiGeorge syndrome, T-negative severe combined immunodeficiency [SCID]) or combined T- and B-cell immunodeficiencies (e.g., T- and B-negative SCID, Wiskott Aldrich syndrome, ataxia telangiectasia, common variable immunodeficiency)
- Any 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 Cancer-Specific Exclusion Criteria
- Any anti-cancer therapy, whether investigational or approved, including chemotherapy, hormonal therapy, and/or radiotherapy, within 3 weeks prior to initiation of study treatment, with the exceptions as mentioned in the protocol
- Eligibility based on prior treatment with CIT depends on the mechanistic class of the drug and the cohort for which the participant is being considered, as described below. In addition, all criteria pertaining to adverse events attributed to prior cancer therapies must be met

All Cohorts (Dose-Escalation in Phase 1a and Dose-Escalation, Backfill, and Expansion in Phase 1b):

- Prior neoantigen-specific or whole-tumor cancer vaccines are not allowed, with the exception as specified in protocol
- Prior treatment with cytokines is allowed provided that at least 6 weeks or 5 half-lives of the drug, whichever is shorter, have elapsed between the last dose and the proposed Cycle 1, Day 1
- Prior treatment with immune checkpoint inhibitors, immunomodulatory monoclonal antibody (mAbs), and/or mAb-derived therapies is allowed provided that at least 6 weeks (Phase 1a) or 3 weeks (Phase 1b) have elapsed between the last dose and the proposed Cycle 1, Day 1, with the exceptions as specified in protocol Phase Ib Dose-Exploration/Expansion Group Only Cohorts
- In the non-melanoma CIT-Naive expansion cohort in Phase Ib, prior treatment with anti-PD-L1/PD-1 and/or anti-CTLA-4 (investigational or approved), is not allowed.

- In the melanoma CIT-naive in metastatic setting expansion cohort in Phase Ib, prior treatment with anti-PD- L1/PD-1 and/or anti-CTLA-4 (investigational or approved) is not allowed. Prior anti-PD-L1/PD-1 and/or anti-CTLA-4 therapy in the adjuvant setting is allowed provided that there is at least a 6-month treatment-free interval between completion of adjuvant therapy and Cycle 1, Day 1.
- Prior treatment with immunomodulators, including toll-like receptor (TLR) agonists, inhibitors of indoleamine 2,3-dioxygenase (IDO)/ tryptophan-2,3-dioxygenase (TDO), or agonists of OX40, is allowed provided that at least 5 half-lives of the drug or a minimum of 3 weeks have elapsed between the last dose of the prior treatment and the proposed Cycle 1, Day 1, with the exception as specified in protocol
- Any history of an immune-mediated Grade 4 adverse event attributed to prior CIT (other than endocrinopathy managed with replacement therapy or asymptomatic elevation of serum amylase or lipase)
- Any history of an immune-mediated Grade 3 adverse event attributed to prior CIT (other than hypothyroidism managed with replacement therapy) that resulted in permanent discontinuation of the prior immunotherapeutic agent and/or occurred less than or equal to (<=) 6 months prior to Cycle 1 Day 1
- Adverse events from prior anti-cancer therapy that have not resolved to Grade <=1 except for alopecia, vitiligo, or endocrinopathy managed with replacement therapy
- All immune-mediated adverse events related to prior CIT (other than endocrinopathy managed with replacement therapy or stable vitiligo) must have resolved completely to baseline
- Primary central nervous system (CNS) malignancy, untreated CNS metastases, or active CNS metastases (progressing or requiring corticosteroids for symptomatic control)
- Leptomeningeal disease
- Uncontrolled tumor-related pain
- Uncontrolled pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures
- Malignancies other than disease under study within 5 years prior to Cycle 1, Day 1, with the exception of those with a negligible risk of metastasis or death
- Uncontrolled hypercalcemia
- Participant has 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 prior to screening

Treatment-Specific Exclusion Criteria:

- History of autoimmune disease with caveats as specified in protocol
- Treatment with monoamine oxidase inhibitors (MAOIs) within 3 weeks prior to Cycle 1, Day 1
- Treatment with systemic immunosuppressive medications within 2 weeks prior to Cycle 1, Day 1
- History of idiopathic pulmonary fibrosis, pneumonitis, organizing pneumonia, or evidence of active pneumonitis on screening chest computed tomography (CT) scan
- Positive test for human immunodeficiency virus (HIV) infection
- Active hepatitis B, hepatitis C
- Known active or latent tuberculosis infection
- Severe infections within 4 weeks prior to Cycle 1, Day 1
- Recent infections not meeting the criteria for severe infections within 2 weeks prior to Cycle 1, Day 1
- Prior allogeneic bone marrow transplantation or prior solid organ transplantation
- Administration of a live, attenuated vaccine within 4 weeks before Cycle 1, Day 1 or anticipation that such a live attenuated vaccine will be required during the study
- Known hypersensitivity to the active substance or to any of the excipients in the vaccine
- Phase 1b and crossover only: History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins; Known hypersensitivity to Chinese Hamster Ovary (CHO)-cell products; Allergy or hypersensitivity to components of the atezolizumab formulation