ForPatients
by Roche

Solid TumorsCancer

A Study of Intravenous (IV) Cergutuzumab Amunaleukin and Atezolizumab in Combination in Participants With Locally Advanced and/or Metastatic Solid Tumors

Trial Status	Trial Runs In	Trial Identifier
Completed	6 Countries	NCT02350673 2014-000948-14 BP29435

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 1b, Open-Label, Multi-Center, Dose Escalation Study of the Safety, Pharmacokinetics, and Therapeutic Activity of Cergutuzumab Amunaleukin, an Immunocytokine, Which Consists of a Variant of Interleukin 2 (IL 2v), That Targets Carcinoembryonic Antigen (CEA), and Atezolizumab, an Antibody That Targets Programmed Death-Ligand 1 (PD-L1), Administered Intravenously, in Patients With Locally Advanced and/or Metastatic Solid Tumors

Trial Summary:

This is an open-label, multi-center, Phase Ib clinical study of cergutuzumab amunaleukin, in combination with atezolizumab, to investigate the safety, pharmacokinetics, and therapeutic activity in participants with locally advanced and/or metastatic carcinoembryonic antigen (CEA)-positive solid tumors, whose disease has progressed on or who are intolerant to the standard of care therapy. Enrolled participants who continue treatment will be treated until loss of clinical benefit, unacceptable toxicities, or withdrawal of consent. The study will include 2 parts: a dose-escalation Part I and a dose expansion Part II. The anticipated treatment period is 24 months for both cergutuzumab amunaleukin and atezolizumab and may be modified if emerging data suggest a benefit.

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Phase 1
Phase

NCT02350673 2014-000948-14 BP29435
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers

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All	# 18 Years	No

Inclusion Criteria:

- Confirmed locally advanced and/or metastatic solid tumor, with at least one tumor lesion of non-critical location accessible to biopsy (with exception of non-small cell lung cancer [NSCLC] participants), and with confirmed progression at baseline that has progressed on, or participant is intolerant to, the standard of care therapy
- Radiologically measurable and clinically evaluable disease as per RECIST v1.1
- Life expectancy, in the opinion of the investigator, greater than or equal to (>=) 12 weeks
- Eastern Cooperative Oncology Group Performance Status 0-1
- 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
- Adequate cardiac, hematological, liver and renal function
- Negative serum pregnancy test within 7 days prior to study treatment in premenopausal women and women <= 2 years 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% per year during the treatment period and for at least five months after the last dose of atezolizumab and at least four months after the last dose of cergutuzumab amunaleukin, whichever is the longest
- For men: agreement to remain abstinent or use contraceptive measures and agreement to refrain from donating sperm
- Locally or centrally confirmed CEA expression in archival tumor tissue
- Participants with unilateral pleural effusion will be eligible for inclusion if they fulfill the Global Initiative for Obstructive Lung Disease classification of 0-1 level for pulmonary function and New York Heart Association (NYHA) classification class 1 for cardiac function

Exclusion Criteria:

- Active or untreated central nervous system (CNS) metastases as determined by computed tomography (CT) or magnetic resonance imaging evaluation during screening and prior radiographic assessments; participants with a history of treated asymptomatic CNS metastases are eligible
- 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 randomization
- Leptomeningeal disease
- Participants with an active second malignancy (other than non-melanoma skin cancer or cervical carcinoma in situ). Participants who have a history of malignancy are not considered to have an active malignancy if they have completed therapy and are considered by their treating physician to be at <= 30 percent (%) risk for relapse
- Evidence of significant, uncontrolled concomitant diseases which could affect compliance with the protocol or interpretation of results, including diabetes mellitus, history of relevant pulmonary disorders, and known autoimmune diseases
- Participants with bilateral pleural effusion and NSCLC participants with uni- or bilateral effusion confirmed at screening by X-ray are not eligible
- Uncontrolled hypertension, unstable angina, congestive heart failure of any NYHA classification stage greater than (>) 2, serious cardiac arrhythmia requiring treatment (exceptions: atrial fibrillation, paroxysmal supraventricular tachycardia), history of myocardial infarction within 6 months of enrollment

- 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. Influenza vaccination should be given during influenza season only. Participants must not receive live, attenuated influenza vaccine within 4 weeks prior to Cycle 1, Day 1, at any time during the study or 5 months after the last dose of atezolizumab
- Known Human Immunodeficiency Virus (HIV)
- Active hepatitis B (HBV) or hepatitis C (HCV) infection
- Severe infections within 4 weeks prior to Cycle 1, Day 1, including but not limited to hospitalization for complications of infection, bacteremia, or severe pneumonia
- Received oral or intravenous (IV) antibiotics within 2 weeks prior to Cycle 1, Day 1. Participants receiving prophylactic antibiotics (for prevention of a urinary tract infection chronic obstructive pulmonary disease) are eligible
- Any other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that would contraindicate the use of an investigational drug
- Major surgery or significant traumatic injury less than (<) 28 days prior to the first cergutuzumab amunaleukin infusion (excluding biopsies) or anticipation of the need for major surgery during study treatment
- Dementia or altered mental status that would prohibit informed consent
- History or risk of autoimmune disease, including but not limited to systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, vascular thrombosis associated with antiphospholipid syndrome, Wegener's granulomatosis, Sjögren's syndrome, Bell's palsy, Guillain-Barré syndrome, multiple sclerosis, vasculitis, or glomerulonephritis
- Participants with a history of autoimmune hypothyroidism on a stable dose of thyroid replacement hormone or participants with controlled Type 1 diabetes mellitus on a stable insulin regimen may be eligible for this study with approval by the medical monitor
- Inclusion of participants with confirmed positive serology of at least one auto-antibody panel (anti-nuclear antibody, anti-double stranded DNA, cytoplasmic anti-neutrophil cytoplasmic antibody, and perinuclear anti-neutrophil cytoplasmic antibody) at screening should be discussed between Sponsor and investigators, and if judged clinically relevant could be referred to a specialist (Rheumatologist) to exclude an underlying auto-immune disease
- History of idiopathic pulmonary fibrosis, pneumonitis (including drug induced), organizing pneumonia (bronchiolitis obliterans, cryptogenic organizing pneumonia), or evidence of active pneumonitis on screening chest CT scan. History of radiation pneumonitis in the radiation field (fibrosis) is permitted
- Baseline QTc interval > 470 milliseconds (ms), baseline resting bradycardia <45 beats per minute (bpm), or baseline resting tachycardia >100 bpm
- Pregnant or breast-feeding women
- Known hypersensitivity to any of the components of cergutuzumab amunaleukin and atezolizumab; hypersensitivity to Chinese hamster ovary cell products or other recombinant human antibodies
- Investigational therapy within 28 days prior to initiation of study treatment
- Any approved anti-cancer therapy, including chemotherapy or hormonal therapy, within 3 weeks prior to initiation of study treatment, with the exceptions stated in the protocol
- Prior corticosteroids as anti-cancer therapy within a minimum of 14 days of first receipt of study drug
- Last dose with any of the following agents including but not limited to: etanercept, infliximab, tacrolimus, cyclosporine, mycophenolic acid, alefacept, or efalizumab <28 days prior to first dose of study drug
- Last dose of prior immunotherapies including but not limited to: interferon alpha, interferon-beta, interleukin (IL)-2, conjugated IL-2, cergutuzumab amunaleukin (CEA-IL2v) , cytokines, anti-cytotoxic T lymphocyte antigen-4, anti-PD-L1, or anti-PD-1 <28 days prior to first cergutuzumab amunaleukin infusion
- History of severe immune-related adverse effects from CEA-IL2v or anti-PD-1 (nivolumab, pembrolizumab) or anti-PD-L1 (atezolizumab) therapies (Common Terminology Criteria for Adverse Events Grade 3 and 4)
- Regular immunosuppressive therapy

- Treatment with systemic immunosuppressive medications including, but not limited to: prednisone, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor agents within 2 weeks prior to Cycle 1, Day 1. Participants who have received acute and/or low-dose systemic immunosuppressant medications may be enrolled in the study after discussion with and approval by the Medical Monitor. The use of inhaled corticosteroids and mineralocorticoids for participants with orthostatic hypotension or adrenocortical insufficiency is allowed
- Radiotherapy within the last 4 weeks before start of study drug treatment with the exception of limited field palliative radiotherapy for bone pain relief