ForPatients
by Roche

Metastatic Colorectal Cancer

Study To Evaluate Safety, Pharmacokinetics, Pharmacodynamics, And Preliminary Anti-Tumor Activity Of RO7122290 In Combination With Cibisatamab With Obinutuzumab Pre-Treatment

Trial Status	Trial Runs In	Trial Identifier
Completed	5 Countries	NCT04826003 BP42675

The clinical trial information herein is sourced from public registries such as ClinicalTrials.gov, EuClinicalTrials.eu, and ISRCTN.com. Additional patient-friendly (lay) content has been prepared by Roche to support understanding.

Official Title:

An Open-Label, Multicenter, Phase Ib Study To Evaluate Safety, Pharmacokinetics, Pharmacodynamics, And Preliminary Anti-Tumor Activity Of RO7122290, A Fibroblast Activation Protein-A (FAP) Targeted 4-1BB Ligand (CD137L), In Combination With Cibisatamab With Obinutuzumab Pre-Treatment, In Participants With Previously Treated, Metastatic, Microsatellite-stable Colorectal Adenocarcinoma With High CEACAM5 Expression

Trial Summary:

This is an open-label, multicenter, Phase Ib study to determine the maximum tolerated dose (MTD) and/or the recommended Phase 2 dose (RP2D) in the weekly (QW) and/or every 3 weeks (Q3W) regimens, safety, tolerability, PK, immunogenicity, PD profile and to evaluate preliminary anti-tumor activity of RO7122290 in combination with cibisatamab Q3W after pretreatment with obinutuzumab, in participants with previously treated metastatic, microsatellite-stable colorectal adenocarcinoma with high CEACAM5 expression

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

NCT04826003 BP42675
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

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Inclusion Criteria:

- Histologically confirmed adenocarcinoma originating from the colon or rectum.
- Metastatic disease (Stage IV American Joint Committee on Cancer, Version 7) not amenable to local treatment.
- Tumors that are MSS (microsatellite-stable) or MSI-low (microsatellite instable low), as determined by a certified laboratory
- Participants with tumors that have high CEACAM5 expression as determined by qRT-PCR in an archival tumor sample or if not available, in a fresh tumor biopsy and documented through central testing of a representative tumor tissue specimen performed at baseline
- Experienced disease progression during or within 3 months following the last administration of approved standard therapies.
- Eastern Cooperative Oncology Group Performance Status of 0 or 1.
- Life expectancy of #12 weeks
- Adequate organ functions.
- Serum creatinine within normal limits or a calculated glomerular filtration rate of # 60 mL/min/1.73 m2 for participants with serum creatinine levels above or below the institutional normal value.
- Serum albumin #30 g/L (3.0 g/dL).
- Lactate dehydrogenase # 2.5 x ULN.
- Adequate contraception

Exclusion Criteria:

- Symptomatic, untreated, or actively progressing central nervous system (CNS) metastases.
- History of leptomeningeal disease
- Non-irradiated tumor lesions > 2 cm at critical sites (e.g., paraspinal, paratracheal, mediastinal, precarnial, sub-glottal) where tumor swelling induced by cibisatamab is expected to lead to significant complications. Irradiation must be completed at least 14 days prior to initiation of study treatment.
- Dyspnea or peripheral capillary oxygen saturation < 92% at rest at baseline for patients with bilateral lung lesions or metastases in the remaining lung following lobectomy or pneumonectomy
- Pleural effusion requiring drainage procedures.
- Pleural effusion and/or pleural lesions involving both lungs
- Active interstitial lung disease (ILD), pneumonitis, or a history of ILD/pneumonitis requiring treatment with steroids or history of idiopathic pulmonary fibrosis, organizing pneumonia (e.g., bronchiolitis obliterans), drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest CT scan.
- History of radiation pneumonitis in the radiation field (fibrosis) is permitted.
- Severe dyspnea at rest due to complications of advanced malignancy or requiring supplementary oxygen therapy.
- Patients with > 10 bilateral pulmonary lesions
- Patients with pulmonary miliary metastatic pattern (innumerable small lesions) or pulmonary lymphangitic carcinomatosis.
- Significant cardiovascular/cerebrovascular disease within 6 months prior to Day 1 of study drug administration
- 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 initiation of study treatment.
- History of progressive multifocal leukoencephalopathy
- Uncontrolled tumor-related pain.
- Uncontrolled ascites requiring recurrent drainage procedures (QW or more frequently). Participants with indwelling catheters are allowed.

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- Patients with pericardial effusion.
- Uncontrolled or symptomatic hypercalcemia
- Active or history of autoimmune disease or immune deficiency, including, but not limited to, myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, antiphospholipid antibody syndrome, Wegener granulomatosis, Sjögren syndrome, Guillain-Barré syndrome, or multiple sclerosis for a more comprehensive list of autoimmune diseases and immune deficiencies).
- Active tuberculosis that has required treatment within 3 years prior to initiation of study treatment or latent tuberculosis that has not been appropriately treated.
- Major surgical procedure, other than for diagnosis, within 4 weeks prior to initiation of study treatment, or anticipation of need for a major surgical procedure during the study.
- History of malignancy other than CRC within 5 years prior to screening, with the exception of malignancies with a negligible risk of metastasis or death (e.g., 5-year OS rate > 90%), such as adequately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, localized prostate cancer, ductal carcinoma in situ, or Stage I uterine cancer.
- 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, or other disease with ongoing fibrosis (such as scleroderma, pulmonary fibrosis, emphysema, neurofibromatosis, palmar/plantar fibromatosis).
- Known active infection, or reactivation of a latent infection, whether bacterial, viral (including, but not limited to, Epstein-Barr virus infection), fungal, mycobacterial, or other pathogens (excluding fungal infections of nail beds), or any major episode of infection requiring hospitalization or treatment with systemic antibiotics (IV and oral antibiotic treatment must have been completed at least 4 and 2 weeks, respectively, prior to initiation of study treatment).
- Prior allogeneic stem cell or solid organ transplantation.
- Any other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding that contraindicates the use of an investigational drug, may affect the interpretation of the results, or may render the patient at high risk from treatment complications.
- Treatment with a live, attenuated vaccine within 4 weeks prior to initiation of study treatment, or anticipation of need for such a vaccine during study treatment.
- 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.
- History of severe allergic or anaphylactic reactions to monoclonal antibody therapy and to chimeric or humanized antibodies or fusion proteins.
- Major surgery or significant traumatic injury < 28 days prior to the first obinutuzumab infusion (excluding biopsies) or anticipation of the need for major surgery during study treatment.
- Treatment with any systemic anti-cancer therapy, including chemotherapy or hormonal therapy, within 28 days prior to initiation of study treatment
- Prior treatment with T-cell bispecifics (TCBs), CD137 (4-1BB) agonists or immune checkpoint blockade therapies, including anti-CTLA-4, anti-PD-1, and anti-PD-L1 therapeutic antibodies, unless discussed and agreed by the Sponsor.
- Treatment with systemic immunostimulatory agents (including, but not limited to, interferon and IL-2) within 4 weeks or 5 half-lives (whatever if longer) prior to initiation of study treatment.
- Treatment with systemic immunosuppressive medication (including, but not limited to, corticosteroids, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-TNF-alpha agents) within 2 weeks prior to initiation of study treatment, or anticipation of need for systemic immunosuppressive medication during study treatment.
- Adverse events from prior anti-cancer therapy that have not resolved to Grade 1 or better with the exception of alopecia of any grade and Grade # 2 peripheral neuropathy.
- Known hypersensitivity to Chinese hamster ovary cell products.
- Known allergy or hypersensitivity to any of the study drugs or any of their excipients.

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- Any participant actively taking anti platelet medication (aspirin, clopidogrel, ticagrelor, etc.) or any participant who is fully anti coagulated with warfarin, low molecular weight heparin or a novel oral anti-coagulant including dabigatran, rivaroxaban, epixaban, etc.
- Pregnancy or breastfeeding, or intention of becoming pregnant during the study.

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