ForPatients
by Roche

Colorectal Cancer (CRC)

A clinical trial to look at how well cibisatamab works in combination with another drug called atezolizumab after pre-treatment with obinutuzumab to treat advanced colorectal cancer (CRC) after chemotherapy has not worked

A phase Ib, multicenter, open-label study to evaluate the safety, efficacy, and pharmacokinetics of cibisatamab in combination with atezolizumab after pretreatment with obinutuzumab in patients with previously treated metastatic, microsatellite-stable colorectal adenocarcinoma with high CEACAM5 expression

Trial Status	Trial Runs In	Trial Identifier
Terminated	4 Countries	NCT03866239 2018-003198-93 CO40939

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 Ib, Multicenter, Open-Label Study to Evaluate the Safety, Efficacy, and Pharmacokinetics of Cibisatamab in Combination With Atezolizumab After Pretreatment With Obinutuzumab in Patients With Previously Treated Metastatic, Microsatellite-Stable Colorectal Adenocarcinoma With High CEACAM5 Expression

Trial Summary:

CO40939 is a Phase Ib, open-label, multicenter, single-arm study designed to evaluate the safety, efficacy, pharmacokinetics, and immunogenicity of cibisatamab in combination with atezolizumab administered after pretreatment with obinutuzumab in patients with Stage IV microsatellite stable (MSS) metastatic colorectal cancer (mCRC) whose tumors have high carcinoembryonic antigen-related cell adhesion molecule 5 (CEACAM5) expression and who have progressed on two or more chemotherapy regimens. The study is composed of a safety run-in and an exploratory part.

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Phase 1
Phase

NCT03866239 2018-003198-93 CO40939
Trial Identifiers

Eligibility Criteria:

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Gender	Age	Healthy Volunteers
All	**#18 Years**	**No**

How does the CO40939 clinical trial work? This clinical trial is recruiting people who have a particular type of colorectal cancer or CRC, which is cancer of the colon or rectum (large intestine or large bowel). In order to take part, patients must have advanced CRC that has spread to other parts of the body (metastatic) and have already tried two or more types of chemotherapy that have not worked.

The purpose of this clinical trial is to test the safety and effectiveness of cibisatamab when given with another drug called atezolizumab after pre-treatment with obinutuzumab, and to understand the way your body processes these medicines.

How do I take part in this clinical trial? To be able to take part in this clinical trial, you must have been diagnosed with advanced CRC (showing high expression of a gene called *CEACAM5*) that has spread to other parts of your body. You must have also been previously treated for your metastatic disease with certain chemotherapy drugs including a fluoropyrimidine, irinotecan and oxaliplatin.

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 must have a very specific type of CRC for this trial so you may have some tests to make sure you will be able to join 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? Everyone who joins this clinical trial will be given:

- A pre-treatment called obinutuzumab, as an infusion (into the vein) as either a single dose or split doses across 2 days, approximately 2 weeks before you start the treatment with cibisatamab and atezolizumab
- On Day 1 of the trial, you will be given
    - atezolizumab as an infusion (into the vein), followed by
    - cibisatamab as an infusion (into the vein)
- You will be given atezolizumab and cibisatamab every 3 weeks until you no longer benefit from the treatment. If your clinical trial doctor thinks it is suitable, you may be allowed to continue treatment with atezolizumab and cibisatamab even after your cancer gets worse

While you are receiving treatment, the clinical trial doctors will check how you are responding to treatment and look for side effects. Patients who experience certain side effects may be treated with a drug called tocilizumab.

How often will I be seen in follow-up appointments, and for how long? You will be given the clinical trial treatment until you no longer benefit from the treatment. You will see the clinical trial doctor regularly throughout the study for a variety of tests and checks to assess how your body is coping with the treatment and ensure it is safe for you to continue. You will also have imaging assessments to see how your cancer is responding to treatment roughly 9 weeks after your first treatment with atezolizumab and cibisatamab and then roughly every 6 weeks after that. Please speak to your doctor if you would like more information on your scheduled visits.

You are free to stop this treatment at any time. After your last treatment, the clinical trial doctor will ask you to come back for a visit within 30 days. After that, your clinical trial doctor will follow up with you, either by phone or hospital visits, every 3 months for the rest of your life (as long as you agree to it). The hospital visits will include blood tests to check whether certain immune cells in your blood have returned to normal levels after stopping treatment.

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 https://clinicaltrials.gov/ct2/show/NCT03866239

Trial-identifier: NCT03866239

Inclusion Criteria:

- Histologically confirmed adenocarcinoma originating from the colon or rectum
- Metastatic disease not amenable to local treatment
- Tumors that are microsatellite stable or microsatellite instability low, as determined by a local, certified laboratory
- Tumors that have high carcinoembryonic antigen-related cell adhesion molecule 5 (CEACAM5) expression as determined by quantitative reverse transcription polymerase chain reaction (qRT-PCR) in an archival tumor sample or 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 hematologic and end-organ function
- Negative HIV test at screening
- Negative hepatitis B surface antigen test and total hepatitis B core antibody (HBcAb) test at screening, or positive total HBcAb test followed by a negative hepatitis B virus (HBV) DNA test at screening
- Negative hepatitis C virus (HCV) antibody test at screening, or positive HCV antibody test followed by a negative HCV RNA test at screening
- Negative human T-cell lymphotropic virus type 1 test for participants from endemic countries (Japan, countries in the Caribbean basin, South America, Central America, sub-Saharan Africa, and Malaysia)
- For women of childbearing potential: agreement to remain abstinent or use contraceptive methods, agreement to regular pregnancy testing, and agreement to refrain from donating eggs, women must remain abstinent or use contraceptive methods with a failure rate of < 1% per year during the treatment period and for 5 months after the final dose of atezolizumab, for 4 months after the final dose of cibisatamab, for 18 months after the final dose of obinutuzumab, and for 3 months after the final dose of tocilizumab
- For men: agreement to remain abstinent or use a condom, and agreement to refrain from donating sperm, with a female partner of childbearing potential or pregnant female partner, men must remain abstinent or use a condom during the treatment period and for 3 months after the final dose of cibisatamab, for 3 months after the final dose of obinutuzumab, and for 2 months after the final dose of tocilizumab to avoid exposing the embryo
- Lactic acid dehydrogenase (LDH) </= 2.5 x upper limit of normal (ULN)

Additional Inclusion Criteria for patient enrollment into Part 2 of the study:

- No prior treatment with regorafenib or Trifluridine/Tipiracil (TAS-102)

Exclusion Criteria:

- Symptomatic, untreated, or actively progressing central nervous system metastases
- Non-irradiated tumor lesions > 2 cm at critical sites where tumor swelling induced by cibisatamab is expected to lead to significant complications
- 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
- 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 leptomeningeal disease and progressive multifocal leukoencephalopathy
- Uncontrolled tumor-related pain and pleural effusion or ascites requiring recurrent drainage procedures

- Participants with pericardial effusion
- Uncontrolled or symptomatic hypercalcemia
- Active or history of autoimmune disease or immune deficiency
- History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography scan
- Active tuberculosis that has required treatment within 3 years prior initiation of study treatment or latent tuberculosis that has not been appropriately treated
- Uncontrolled hypertension, unstable angina, congestive heart failure of any New York Heart Association Class II or greater, serious cardiac arrhythmia requiring treatment and history of myocardial infarction within 6 months prior to initiation of study treatment
- 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, 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
- Known active infection, or reactivation of a latent infection, whether bacterial, viral, fungal, mycobacterial, or other pathogens, or any major episode of infection requiring hospitalization or treatment with IV antibiotics
- 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 or within 5 months after the final dose of atezolizumab
- Current treatment with anti-viral therapy for HBV
- Treatment with any systemic anti-cancer therapy, including chemotherapy or hormonal therapy, within 28 days prior to initiation of study treatment
- Treatment with investigational therapy within 28 days prior to initiation of study treatment
- Prior treatment with any of the protocol-specified study treatments
- Prior treatment with T-cell bispecifics (TCBs), including CEACAM5-TCB, CD137 agonists or immune checkpoint blockade therapies, including anti-CTLA-4, anti-PD-1, and anti-PD-L1 therapeutic antibodies
- Treatment with systemic immunostimulatory agents within 4 weeks or 5 half-lives of the drug prior to initiation of study treatment
- Treatment with systemic immunosuppressive medication 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
- History of severe allergic anaphylactic reactions to chimeric or humanized antibodies or fusion proteins
- Known hypersensitivity to Chinese hamster ovary cell products
- Known allergy or hypersensitivity to any of the study drugs or any of their excipients
- Pregnancy or breastfeeding, or intention of becoming pregnant during study treatment or within 5 months after the final dose of atezolizumab, within 4 months after the final dose of cibisatamab, within 18 months after the final dose of obinutuzumab, and within 3 months after the final dose of tocilizumab
- Participants with pleural effusion requiring drainage procedures
- Participants with pleural effusion and/or pleural lesions involving both lungs (i.e. bilateral pleural effusions; unliateral pleural effusion with pleural lesion in the contralateral lung)
- Participants with >10 bilateral pulmonary lesions (i.e. at least one lesion in each lung and more than 10 lung lesions in total)
- Participants with pulmonary miliary metastatic pattern (innumerable small lesions) or pulmonary lymphangitic carcinomatosis