ForPatients
by Roche

Multiple Myeloma

A clinical trial to look at how safe and well cevostamab works in people with multiple myeloma after other treatments have not worked

A Study Evaluating the Efficacy and Safety of Cevostamab in Prior B Cell Maturation Antigen (BCMA)-Exposed Participants With Relapsed/Refractory Multiple Myeloma

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	8 Countries	NCT05535244 2021-006816-10 CO43476

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 I/II, Open-Label, Multi-Cohort Study to Evaluate the Efficacy and Safety of Cevostamab in Prior B Cell Maturation Antigen-Exposed Patients With Relapsed/Refractory Multiple Myeloma

Trial Summary:

This study will evaluate the efficacy, safety, and pharmacokinetics of cevostamab in participants with relapsed or refractory multiple myeloma (R/R MM) via intravenous (IV) infusion.

Hoffmann-La Roche
Sponsor

Phase 1/Phase 2
Phase

NCT05535244 2021-006816-10 CO43476
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is the CAMMA 2 clinical trial needed?

Multiple myeloma (MM) is a type of bone marrow cancer. In cases where a person's cancer comes back after treatment (relapsed MM) or does not respond to treatment (refractory MM), other treatment options are needed. Cevostamab is a type of drug called a T-cell dependent bispecific antibody. It works by binding to certain proteins on myeloma

cells and cells of the immune system to bring them closer together to help the immune system destroy the myeloma cells. Drugs like cevostamab, called immunotherapies, help a person's own immune system target and destroy cancer cells. Researchers hope that immunotherapies will provide better health outcomes for people with relapsed or refractory MM. This clinical trial aims to find out the effects, good or bad, of cevostamab and to understand the way the body responds to and processes cevostamab in people with relapsed or refractory MM.

2. How does the CAMMA 2 clinical trial work?

This clinical trial is recruiting people with relapsed or refractory MM. People who take part in this clinical trial (participants) will be given the clinical trial treatment cevostamab for as long as it can help them or until they are unable to tolerate the treatment due to side effects (unexpected medical problems). Participants will stay in the hospital for observation for at least 48 hours after the first three doses of cevostamab, with the first two doses given 1–3 days apart (depending on how they tolerate the treatment) in a single visit. Future doses may be given on an outpatient basis and the clinical trial doctor will see them every 3 weeks. These hospital visits will include checks to see how the participant responds to the treatment and any side effects they may have. If cevostamab treatment is stopped due to MM getting worse, an end of treatment visit will take place 30 days after the last dose, and the clinical trial doctor will follow up with participants approximately every 3 months until the end of the clinical trial for as long as they agree to it. If cevostamab treatment is stopped for any other reason, the clinical trial doctor will follow-up with participants approximately every month for as long as they agree to it and until MM gets worse, they start a new treatment for MM, or the clinical trial ends. The total time of participation in the clinical trial will depend on how their MM responds to treatment. This could range from 1 day to more than 4 years. Participants can stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the CAMMA 2 clinical trial?

The main clinical trial endpoints (the main results measured in the trial to see if the drug has worked) are how many participants' cancer shows a positive response to treatment and how good this response is (objective response rate), and the number and seriousness of any side effects that occur while on treatment.

The other clinical trial endpoints include:

- The amount of time between cancer getting better from treatment and then getting worse (duration of response)
- The number of people with no signs of cancer on scans or tests (complete response rate)
- The number of people with at least a 90% improvement in their disease (very good partial response)

- The amount of time between the start of the trial to cancer first getting better, and to the best response to treatment
- The number of people with no disease detected after treatment
- How long people live (overall survival)
- How long people live without their cancer worsening (progression-free survival)
- Levels of cevostamab in the blood at different time points
- Number of people with less tiredness and better quality of life

4. Who can take part in this clinical trial?

People can take part in this trial if they are at least 18 years old, have been diagnosed with relapsed or refractory MM and have previously received treatment with certain cancer immunotherapies that target a part of myeloma cells called BCMA (including CAR-T, antibody-drug conjugate, and T-cell dependent bispecific antibody therapies). People may not be able to take part in this trial if they have received previous treatment with cevostamab or certain other treatments, have certain other medical conditions, are pregnant or breastfeeding, or are planning to become pregnant during or shortly after the trial.

5. What treatment will participants be given in this clinical trial?

Everyone who joins this clinical trial will be given cevostamab as an intravenous infusion (into the vein). The clinical trial is split up into periods called ‘cycles’, each lasting 21 days:

- In Cycle 1, participants will receive step-up (or increasing) doses of cevostamab on Day 1, Days 2#4, and Day 8 (target dose reached on Day 8)
- From Cycle 2, participants will receive cevostamab once every 21 days at the target dose

Step-up dosing aims to prevent and/or reduce side effects. If a participant experiences a potential side effect called ‘cytokine release syndrome’ (when the body’s immune cells release large amounts of inflammatory substances throughout the body), they may receive another drug called tocilizumab. This is an open-label trial, which means everyone involved, including the participant and the clinical trial doctor, will know the clinical trial treatment the participant has been given.

6. Are there any risks or benefits in taking part in this clinical trial?

The safety or effectiveness of the experimental treatment or use may not be fully known at the time of the trial. Most trials involve some risks to the participant. However, it may not be greater than the risks related to routine medical care or the natural progression of the health condition. People who would like to participate will be told about any risks and benefits of taking part in the clinical trial, as well as any additional procedures, tests, or assessments they will be asked to undergo. All of these will be described in an informed

consent document (a document that provides people with the information they need to decide to volunteer for the clinical trial).

Risks associated with the clinical trial drug

Participants may have side effects (an unwanted effect of a drug or medical treatment) from the drug used in this clinical trial. Side effects can be mild to severe, even life-threatening, and vary from person to person. Participants will be closely monitored during the clinical trial; safety assessments will be performed regularly. Cevostamab and tocilizumab will be given by intravenous infusion (into a vein). Participants will be told about any known side effects of intravenous infusions.

Potential benefits associated with the clinical trial

Participants' health may or may not improve from participation in the clinical trial. Still, the information collected may help other people with similar medical conditions in the future.

Inclusion Criteria:

- Documented diagnosis of MM based on standard International Myeloma Working Group (IMWG) criteria
- Evidence of progressive disease based on investigators determination of response by IMWG criteria on or after their last dosing regimen
- Prior BCMA ADC or CAR-T Cohort: participants who have received a BCMA-targeted CAR-T or ADC therapy and are triple-class relapsed or refractory
- Prior BCMA Bispecific Cohort: participants who have received a BCMA-targeting T-cell-dependent bispecific (TDB) antibody and are triple-class relapsed or refractory
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1
- Life expectancy is at least 12 weeks
- Agreement to protocol-specified assessments, including bone marrow biopsy and aspirate samples as detailed in the protocol
- Resolution of AEs from prior anti-cancer therapy to Grade =< 1
- For female participants of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraception during the treatment period and for at least 5 months after the final dose of cevostamab and for 3 months after the last dose of tocilizumab was administered
- For male participants: agreement to remain abstinent (refrain from heterosexual intercourse) or use a condom, and agree to refrain from donating sperm during the treatment period and for at least 2 months after the final dose of tocilizumab (if applicable) to avoid exposing the embryo

Exclusion Criteria:

- Inability to comply with protocol-mandated hospitalization
- Pregnancy or breastfeeding, or intention of becoming pregnant during the study or within 5 months after the final dose of cevostamab or tocilizumab or within 3 months after the last dose of tocilizumab (if applicable)
- Prior treatment with cevostamab or another agent with the same target
- Prior BCMA ADC or CAR-T Cohort: prior treatment with any T cell dependent bi-specific antibody (TDB) antibody including non BCMA targeting TDB

- Prior use of any monoclonal antibody (mAb), radioimmunoconjugate, or ADC as anti-cancer therapy within 4 weeks before first study treatment, except for the use of non-myeloma therapy
- Prior treatment with systemic immunotherapeutic agents
- Prior treatment with CAR-T cell therapy within 12 weeks before first cevostamab infusion
- Known treatment-related, immune-mediated adverse events associated with prior checkpoint inhibitors
- Treatment with radiotherapy, any chemotherapeutic agent, or treatment with any other anti-cancer agent within 4 weeks or 5 half-lives of the drug, whichever is shorter, prior to first study treatment
- Autologous stem cell transplantation (SCT) within 100 days prior to first study treatment
- Prior allogeneic SCT
- Circulating plasma cell count exceeding 500/ microliter (µL) or 5% of the peripheral blood white cells
- Prior solid organ transplantation
- History of autoimmune disease
- History of confirmed progressive multifocal leukoencephalopathy
- History of severe allergic or anaphylactic reactions to mAb therapy
- Known history of amyloidosis
- Lesions in proximity of vital organs that may develop sudden decompensation/deterioration in the setting of a tumor flare
- History of other malignancy within 2 years prior to screening, except those with negligible risk of metastasis or death, such as ductal carcinoma in situ not requiring chemotherapy, appropriately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, low-grade, localized prostate cancer not requiring treatment or appropriately treated Stage I uterine cancer
- Current or past history of central nervous system (CNS) disease, such as stroke, epilepsy, CNS vasculitis, neurodegenerative disease, or CNS involvement by MM
- Significant cardiovascular disease that may limit a potential participant's ability to adequately respond to a cytokine release syndrome (CRS) event
- Symptomatic active pulmonary disease or requiring supplemental oxygen
- Known active bacterial, viral, fungal, mycobacterial, parasitic, or other infection at study enrollment, or any major episode of infection requiring treatment with IV (intravenous) antimicrobials where the last dose of IV antimicrobial was given within 14 days prior to first study treatment
- Active symptomatic COVID-19 infection at study enrollment or requiring treatment with IV antiviral where the last dose of IV antiviral treatment was given within 14 days prior to first study treatment. Participants with active COVID-19 infection must have clinical recovery and two negative antigen tests at least 24 hours apart prior to first study treatment
- Positive and quantifiable Epstein-Barr virus (EBV) polymerase chain reaction (PCR) or cytomegalovirus (CMV) PCR prior to first study treatment
- Known or suspected chronic active EBV infection
- Known history of Grade >=3 CRS or immune effector cell-associated neurotoxicity syndrome (ICANS) with prior bispecific therapies
- Known history of hemophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS)
- Recent major surgery within 4 weeks prior to first study treatment
- Positive serologic or PCR test results for acute or chronic hepatitis B virus (HBV) infection
- Acute or chronic hepatitis C virus (HCV) infection
- Known history of human immunodeficiency virus (HIV) seropositivity
- Administration of a live, attenuated vaccine within 4 weeks before first study treatment or anticipation that such a live attenuated vaccine will be required during the study
- Treatment with systemic immunosuppressive medications, with the exception of corticosteroid treatment <= 10 mg/day prednisone or equivalent, within 2 weeks prior to first study treatment
- History of illicit drug or alcohol abuse within 12 months prior to screening, in the investigator's judgment
- 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, or which could affect compliance with the protocol or interpretation of results