ForPatients
by Roche

Multiple Myeloma

A study to look at the safety of cevostamab alone, and in combination with other treatments in people with relapsed or refractory multiple myeloma

A Study Evaluating the Safety, Pharmacokinetics, and Activity of Cevostamab in Participants With Relapsed or Refractory Multiple Myeloma

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	13 Countries	NCT04910568 2023-507019-36-00 GO42552

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:

An open-label, multicenter, phase Ib trial evaluating the safety, pharmacokinetics, and activity of cevostamab as monotherapy and cevostamab plus pomalidomide and dexamethasone or cevostamab plus daratumumab and dexamethasone in patients with relapsed or refractory multiple myeloma

Trial Summary:

This Phase Ib, multicenter, open-label study will evaluate the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of cevostamab monotherapy, cevostamab plus pomalidomide and dexamethasone (Pd) or cevostamab plus daratumumab and dexamethasone (Dd) which will be administered to participants with relapsed or refractory multiple myeloma (R/R MM) via intravenous (IV) infusion.

Genentech, Inc.
Sponsor

Phase 1
Phase

NCT04910568 2023-507019-36-00 GO42552
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is this study needed?

Multiple myeloma (MM) is a type of cancer that affects plasma cells in the bone marrow. Plasma cells are a type of white blood cell that helps fight infection. In MM, these plasma cells become cancerous. They multiply rapidly and crowd out healthy cells in the bone marrow. Different types of medicines are given as standard-of-care treatment depending on the type of MM a person has. This includes protease inhibitors (PIs) or 'immunotherapy'. Immunotherapy is medicine that help a person's own immune system target and destroy cancer cells. Medicines called 'IMiDs' and 'anti-CD38' are immunotherapies. MM can be refractory – when it does not respond to standard treatments. Or MM can relapse – the return of signs, symptoms, or a disease after they have improved for a while. This is known as 'relapsed/refractory' or 'R/R' MM. New treatments are needed for people with R/R MM.

This study is testing a medicine called cevostamab alone or in combination with pomalidomide and dexamethasone (Pd), or daratumumab and dexamethasone (Dd). They are being developed to treat R/R MM.

Cevostamab alone or in combination with Pd or Dd are experimental medicines in this study. This means health authorities have not approved these combinations for the treatment of R/R MM. Pomalidomide is approved to treat R/R MM when it is combined with certain other medicines. But only after one or two prior treatments for MM. Daratumumab is approved to treat MM when it is combined with certain other medicines as a first treatment for MM, and after one or two prior treatments for MM. Daratumumab on its own is also approved to treat MM after at least 3 prior lines of therapy.

This study aims to test how safe cevostamab alone and in combination with Pd or Dd and to understand what happens to cevostamab once it is in the body.

2. Who can take part in the study?

People 18 years of age or older with relapsed or refractory MM can take part in the study if they have not been treated with cevostamab or a similar drug before.

People may not be able to take part in this study if they have had certain medical conditions such as heart or lung conditions or they have had some certain treatments. People who are pregnant, planning to become pregnant, or currently breastfeeding cannot take part in the study.

3. How does this study work?

People will be screened to check if they are able to participate in the study. The screening period will take place from 4 weeks before the start of treatment.

Everyone in this study will be given cevostamab, as a drip into a vein with or without other study medicines. Participants will join 1 of 3 treatment groups depending on what

medicines they have had before. Cevostamab will be given more often at the start of treatment — known as ‘step up doses. Step up doses start with a lower dose and then progressively increase dosage over time. Treatment will be given cycles. A treatment cycle is the period of treatment and recovery time before the next set of treatment is given.

Group A:

- Cevostamab given every 1, 2 then 4 weeks

Group B:

- Cevostamab given as step up doses over 3 weeks in a ‘pre-treatment’ phase. Cevostamab will then be given every 2 or 4 weeks
- Pomalidomide, as a pill to be swallowed daily for 3 weeks in each cycle
- Dexamethasone, as a pill to be swallowed or as a drip into a vein given weekly in Cycles 1 to 4. Dexamethasone may be given 3 to 4 times during the ‘pre-treatment’ phase. Dexamethasone may not be given after Cycle 4

Group C:

- Cevostamab given every 1, 3 then 4 weeks. In Cycle 1, 2 step up doses may also be given
- Daratumumab, as an injection under the skin. Daratumumab will be given 3 times during Cycles 1 to 3, then every 3 weeks, then every 4 weeks
- Dexamethasone, as a pill to be swallowed or as a drip into a vein. Dexamethasone will be given every 1, 3 then 4 weeks. In Cycle 1, more doses may be given. Dexamethasone may not be given after Cycle 5

Participants may also receive tocilizumab as a drip into a vein if they experience certain unwanted effects such as an immune reaction (known as ‘cytokine release syndrome’). This is an open-label study. This means everyone involved, including the participant and the study doctor, will know the study treatment the participant has been given.

During this study, the study doctor will see participants every 1 to 2 weeks and then on Day 1 of later cycles. They will see how well the treatment is working and any unwanted effects participants may have. Participants will have follow-up visit/s or receive telephone calls from the study doctor every 3 months of completing the study treatment, during which the study doctor will check on the participant’s wellbeing. Total time of participation in the study could be more than 1 year. Participants have the right to stop study treatment and leave the study at any time, if they wish to do so.

4. What are the main results measured in this study?

The main result measured in the study is the number, type and seriousness of unwanted effects of cevostamab given on its own or in combination with other study medicines.

Other key results measured in the study include:

- How many people have a reduction of their cancer after treatment
- The number of people who do not have cancer on tests or scans after treatment
- The number of people with a significant improvement or better in the health condition being treated
- How long people live without their cancer getting worse
- How much time there is between the person's cancer first responding to treatment and the cancer getting worse
- How much time there is between starting the study treatment and the cancer first responding, and when does it best respond in people with cancer that has reduced by half
- The number of participants have at least a 90% reduction in cancer on tests or scans after treatment
- How long people live
- How the study medicines get to different parts of the body, and how the body changes and gets rid of it

5. Are there any risks or benefits in taking part in this study?

Taking part in the study may or may not make participants feel better. But the information collected in the study can help other people with similar health conditions in the future. It may not be fully known at the time of the study how safe and how well the study treatment works. The study involves some risks to the participant. But these risks are generally not greater than those related to routine medical care or the natural progression of the health condition. People interested in taking part will be informed about the risks and benefits, as well as any additional procedures or tests they may need to undergo. All details of the study will be described in an informed consent document. This includes information about possible effects and other options of treatment.

Risks associated with the study drugs

Participants may have unwanted effects of the drugs used in this study. These unwanted effects can be mild to severe, even life-threatening, and vary from person to person. During this study, participants will have regular check-ups to see if there are any unwanted effects.

Cevostamab, pomalidomide, daratumumab, dexamethasone and tocilizumab

Participants will be told about the known unwanted effects of cevostamab, pomalidomide, daratumumab, dexamethasone, and tocilizumab, and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects include immune reaction, increased risk of infection, rash, frequent watery stools, wanting to throw up, pain or discomfort in the head, confusion, low number of white blood cells, throwing up, blood clots, liver toxicity, and shortness of breath.

Known unwanted effects of injections under the skin and drips into a vein include throwing up, wanting to throw up, a feeling of coldness that makes the body shiver, low or high blood pressure, fever, pain or discomfort in the head, frequent watery stools, shortness of breath, and cough. The study medicine(s) may be harmful to an unborn baby. Women and men must take precautions to avoid exposing an unborn baby to the study treatment.

Inclusion Criteria:

- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1
- Life expectancy of at least 12 weeks
- Agreement to provide bone marrow biopsy and aspirate samples
- Resolution of adverse events from prior anti-cancer therapy to Grade <=1
- Measurable disease
- For women of childbearing potential: agreement to remain abstinent or use contraception, during the treatment period (including treatment interruptions) and for at least 5 months after the last dose of cevostamab and at least 3 months after the last dose of tocilizumab was administered
- For men: agreement to remain abstinent or use a condom, and agreement to refrain from donating sperm, during the treatment period, and for at least 2 months after the last dose of tocilizumab was administered to avoid exposing the embryo and sexual partner Additional Arm A-Specific Inclusion Criteria
- Diagnosis of R/R MM for which no established therapy for MM is appropriate and available, or intolerance to those established therapies Additional Arm B-Specific Inclusion Criteria
- For Cohort B1S: Participants with R/R MM who have received at least two prior lines of treatment
- For Cohort B2S and additional cohorts: Participants with R/R MM who have received at least 1 prior line of treatment
- Agreement to comply with all requirements of the pomalidomide pregnancy prevention program
- For women of childbearing potential: agreement to remain abstinent or use two reliable methods of contraception starting at least 4 weeks prior to, during the treatment period, and for at least 4 weeks after the last dose of pomalidomide was administered
- For men: agreement to remain abstinent or use a condom during the treatment period and for at least 4 weeks after the last dose of pomalidomide, (even if he has undergone a successful vasectomy) and agreement to refrain from donating sperm and blood during this same period Additional Arm C-Specific Inclusion Criteria
- For Cohort C1S: Participants with R/R MM who have received at least two prior lines of treatment
- For Cohort C2S and additional cohorts: Participants with R/R MM who have received at least 1 prior line of therapy
- For women of childbearing potential: agreement to remain abstinent or use contraceptive methods during the treatment period and for at least 102 days after the last dose of daratumumab was administered
- For men: agreement to remain abstinent or use a condom during the treatment period and for at least 102 days after the last dose of daratumumab was administered to avoid exposing the embryo, and agreement to refrain from donating sperm during this same period

Exclusion Criteria:

- Prior treatment with cevostamab or another agent targeting FcRH5
- Inability to comply with protocol-mandated hospitalization and activities restrictions
- Pregnant or breastfeeding, or intending to become pregnant during the study or within 5 months after the last dose of cevostamab or within 3 months after the last dose of tocilizumab (if applicable).

- Prior use of any monoclonal antibody, radioimmunoconjugate, or antibody-drugconjugate 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, including, but not limited to, cytokine therapy and anti-CTLA4, anti-PD-1, and antiPD-L1 therapeutic antibodies within 12 weeks or 5 half-lives of the drug, whichever is shorter, before first study treatment
- Prior treatment with chimeric antigen receptor T (CAR T)-cell therapy within 12 weeks before first study treatment
- Treatment with radiotherapy within 4 weeks (systemic radiation) or 14 days (focal radiation) prior to first study treatment
- Treatment with any chemotherapeutic agent or other anti-cancer agent (investigational or otherwise) within 4 weeks or 5 half-lives of the drug, whichever is shorter, prior to first study treatment
- Autologous SCT within 100 days prior to first study treatment
- Prior allogeneic stem cell transplant(ation) (SCT)
- Circulating plasma cell count exceeding 500/micro L 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 monoclonal antibody 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
- Known treatment-related, immune-mediated adverse events associated with prior checkpoint inhibitors
- 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
- Symptomatic active pulmonary disease or requiring supplemental oxygen
- Known active bacterial, viral, fungal, mycobacterial, parasitic, or other infection
- Known or suspected chronic active Epstein-Barr virus (EBV) infection
- 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 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)
- Active symptomatic coronavirus disease 2019 (COVID-19) infection at study enrollment or requiring treatment with intravenous (IV) antiviral where the last dose of IV antiviral treatment was given within 14 days prior to first study treatment. Patients 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 EBV polymerase chain reaction (PCR) or Cytomegalovirus (CMV) PCR prior to first study treatment
- Known history of 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 Additional Arm B-Specific Exclusion Criteria
- Pregnant or breastfeeding, or intending to become pregnant 4 weeks prior to initiation of study treatment, during the study, (including treatment interruptions) or within 4 weeks after the last dose of pomalidomide

- Significant cardiovascular disease (such as, but not limited to, New York Heart Association Class III or IV cardiac disease, myocardial infarction within the last 12 months, uncontrolled arrhythmias, or unstable angina)
- History of erythema multiforme, Grade >=3 rash, blistering, or severe hypersensitivity to prior treatment with immunomodulatory drugs such as thalidomide, lenalidomide, or pomalidomide
- Inability to tolerate thromboprophylaxis, or contraindication to thromboprophylaxis
- GI disease that might significantly alter absorption of oral drugs Additional Arm C-Specific Exclusion Criteria
- Pregnant or breastfeeding, or intending to become pregnant during the study or within 102 days after the last dose of daratumumab
- Known hypersensitivity to biopharmaceuticals produced in CHO cells or any component of daratumumab formulations
- Known chronic obstructive pulmonary disease (COPD) with a forced expiratory volume in 1 second (FEV1) <50% of predicted normal
- Known moderate or severe persistent asthma within the past 2 years, or current uncontrolled asthma of any classification