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Study evaluating the safety and activity of cevostamab (BFCR4350A) given by subcutaneous injection in participants with relapsed or refractory multiple myeloma

Submission date
30/11/2021

Recruitment status
No longer recruiting

Registration date
08/12/2021

Overall study status
Ongoing

Last Edited
09/06/2025

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Multiple myeloma (MM) is an incurable cancer affecting the plasma cells in the bone marrow (a soft tissue found inside most of the bones that produce blood cells). Plasma cells are a type of white blood cell that produce certain proteins that helps the body fight diseases and infections. The main symptoms of MM include increased blood calcium levels, kidney failure, a decrease in red blood cell count, and bone damage. Eventually, most patients either experience disease worsening (relapse) after a temporary improvement in symptoms or develop refractory MM (MM that is resistant to treatment). This is collectively known as relapsed or refractory MM (R/R MM). Cevostamab subcutaneous (SC; injected under the skin) is an experimental drug, which means health authorities have not approved it for the treatment of multiple myeloma. The main aims of this study are:
1. To assess the safety and tolerability of cevostamab SC, to find out the highest dose of cevostamab SC that a participant can tolerate, and to identify any toxicities that may prevent the study doctors from further increasing the dose of the study drug
2. To identify the best dose of cevostamab SC for the next phase (Phase II) of the study
3. To make an initial assessment of the amount of disease response that cevostamab SC produces.
4. To describe how cevostamab SC will be distributed and eliminated from the body.

Who can participate?
Patients who are over 18 years of age and have a confirmed diagnosis of R/R MM

What does the study involve?
Participants may be asked to be in the study for about 12 months depending on how well they tolerate the drug and whether they qualify for re-treatment (re-start of treatment). The study has three parts:
1. A screening period of up to 28 days before the start of the study where tests will be done to check if the participants are eligible to take part in the study.

2. A treatment period where participants will have to check into a hospital to receive the first three or four doses of cevostamab SC so that they can be monitored for possible side effects. They will have to stay in the hospital for observation for at least 72 hours after receiving the drug. In case of certain side effects with the initial doses, participants may need to receive the subsequent dose(s) in the hospital as well. Once participants tolerate cevostamab SC without experiencing certain side effects, future doses will be administered on an outpatient basis, with participants being required to stay and be monitored for at least 90 minutes after each dose before being discharged.
3. A follow-up period where participants who complete 13 cycles (1 cycle is 28 days) will be followed-up for tumour and additional assessments until worsening of disease, the start of new anti-cancer therapy, or withdrawal from study participation, whichever occurs first.

The study will be conducted in two stages:
1. Dose escalation stage: Dose escalation means that participants in one group will receive study treatment at a certain dose and once this dose is considered tolerable, the next group of participants will receive a higher dose. A participant's dose will be increased if the doctors think that the treatment is beneficial and side effects are manageable. During the first cycle (28 days) of the study, participants will receive cevostamab SC injected into the abdomen on Days 1, 8, and 15 for a total of three doses. The doses will be administered, for most participants, in rotating spots on their abdomen, and the doses will be gradually increased in amount to the largest dose on Day 15. If in some cases the study doctor decides that doses into the abdomen are to be avoided, then doses will be given at different areas under the skin of the thighs instead. If the participants are responding well to cevostamab SC and their MM is not worsening, they will continue receiving cevostamab SC every 2 weeks (Q2W) for 11 more doses, then every 4 weeks (Q4W) thereafter for six doses.

2. Dose expansion stage: This stage will further assess the safety and tolerability of cevostamab SC. The dose for the dose-expansion stage will be based on the findings of the dose-escalation stage. Participants will receive cevostamab SC injected into the abdomen on Days 1, 4, 8, and 11 for a total of four doses in Cycle 1 (lasting 21 days). The doses will be administered, for most participants, in rotating spots on their abdomen, and the doses will be gradually increased in amount to the largest dose on Day 11. If in some cases the study doctor decides that doses into the abdomen are to be avoided, then doses will be given at different areas under the skin of the thighs instead. If the participants are responding well to cevostamab SC and their MM is not worsening, they will continue receiving cevostamab SC Q2W for 11 more doses in 28-day cycles, then Q4W thereafter for 6 doses in 28-day cycles.

To help prevent side effects from cevostamab SC, participants will receive a pain reliever/fever reducer (acetaminophen), and an anti-allergic (diphenhydramine or a similar medication) before every injection of cevostamab SC. In addition to these a corticosteroid (dexamethasone or a similar medication) will be given before the first five doses (and maybe more depending on whether participants experience certain side effects).

Re-treatment: Participants who have a good response to cevostamab SC treatment but experience a worsening of MM after stopping cevostamab SC treatment may be eligible to restart treatment (re-treatment) with cevostamab SC. Re-treatment would begin with hospitalisation (as described above) and may continue until their MM worsens or they experience certain side effects.

What are the possible benefits and risks of participating?
Participants may not receive any benefit from participating in this study, but the information that is learned may help people with certain cancers in the future.

Participants may have side effects from the drugs or procedures used in this study that are mild to severe and even life-threatening, and they can vary from person to person. The potential side effects related to the study drug, based on laboratory studies or knowledge of similar drugs, are listed below:
1. Cytokine release syndrome (CRS): this is an inflammatory response that is triggered by certain infections and drugs
2. Dyspnea (difficulty breathing)
3. Increased risk of infection
4. Reaction to the injection that affects the whole body (also known as a systemic injection-related reaction), with symptoms such as fever, chills, rash, low blood pressure, nausea, cold-like symptoms, and shortness of breath
5. Injection-site reaction, which could include pain, tenderness, swelling, redness, warmth, and itching at the injection site
6. Low blood pressure
7. Headache
8. Dizziness
9. Tremor
10. Problems with walking
11. Problems with speech
12. Confusion
13. Seizures
14. Low platelets (cells that help clot blood)
15. Rash
16. Decreased numbers of white blood cells (cells that help fight infections)
17. Elevation in liver enzymes, which may indicate liver damage
18. Tumor lysis syndrome (rapid release of substances from dying cancer cells that could be harmful to the body)
19. Pain in tumor sites
20. Tumor inflammation (symptoms of tumor swelling, such as pain at the tumor sites, which may require additional medical or surgical treatment [for example, anti-inflammatory medicines, invasive procedure, or prolonged hospitalization]).
21. Development of special antibodies (proteins made in the body that respond to a substance that is foreign to the body)
22. Hemophagocytic lymphohistiocytosis (HLH) / macrophage activation syndrome (MAS): this is a rare, life-threatening condition when the immune system does not work normally, because certain white blood cells (lymphocytes and histiocytes) attack the other blood cells. These abnormal blood cells collect in the spleen and liver, causing these organs to enlarge. Other symptoms can include fevers, swollen lymph nodes, skin rashes, yellowing of the skin and eyes [jaundice], coughing, difficulty breathing, vomiting, diarrhea, headache, trouble walking, trouble seeing, and general weakness)
There may be a risk in exposing an unborn child to the study drug, and all risks are not known at this time. Women and men must take precautions to avoid exposing an unborn child to the study drug. Women who are pregnant, have become pregnant, or are currently breastfeeding, cannot take part in this study.

Where is the study run from?
Genentech Inc. (USA)

When is the study starting and how long is it expected to run for?
May 2021 to November 2026

Who is funding the study?
Genentech Inc. (USA)

Who is the main contact?
global.trial_information@roche.com

Contact information

Type(s)
Public

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
GO43227

Study information

Scientific Title
A phase Ib, open-label, multicenter, trial evaluating the safety, pharmacokinetics, and activity of subcutaneous cevostamab (BFCR4350A) in patients with relapsed or refractory multiple myeloma (CAMMA 3)

Acronym
CAMMA 3

Study objectives
Current study hypothesis:
To evaluate the safety and tolerability of SC cevostamab, including estimation of the maximum tolerated dose (MTD), characterization of dose-limiting toxicity (DLTs), and to identify the recommended phase II dose (RP2D) of SC cevostamab in participants with R/R MM.

Previous study hypothesis:
To evaluate the safety and tolerability of subcutaneous (SC) cevostamab, including estimation of the maximum tolerated dose (MTD), characterization of dose-limiting toxicity (DLTs), and to

identify the recommended phase II dose (RP2D) of SC cevostamab in participants with relapsed or refractory multiple myeloma (R/R MM).

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 16/07/2021, Hellenic Republic Ministry of Health, National Ethics Committee (284 Mesogeion Ave, Cholargos, 155 62, Greece; +30 (0)213 2040259 ext 554; eed@eof.gr), ref: 62423 /2021

Study design
Phase Ib multicenter open-label dose-escalation and dose-expansion study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Multiple myeloma

Interventions
Current interventions as of 09/06/2025:

Arm A: Dose-escalation cohorts:
Participants will receive cevostamab SC, with step-up dosing on Days 1 and 8 of Cycle 1 (the duration of each cycle is 28 days) and then at the target dose on Day 15 in Cycle 1. From Cycle 2 onwards participants will receive cevostamab at the target dose, SC, Q2W on Days 1 and 15 in Cycles 2 to 6, and thereafter Q4W on Day 1 from Cycles 7 up to a maximum of 13 cycles, or until disease progression, or unacceptable toxicity, whichever occurs first.

Arm A: Dose-expansion cohorts:
Participants will receive cevostamab SC, with step-up dosing on Days 1, 4 and 8 of Cycle 1 (Cycle 1 lasting 21 days) and then at the target dose on Day 11 of Cycle 1. From Cycles 2 to 6 (Cycle length = 28 days) onwards, participants will receive cevostamab at the target dose,

SC, Q2W on Days 1 and 15 and thereafter Q4W on Day 1 from Cycle 7 up to a maximum of 13 cycles, or until disease progression, or unacceptable toxicity, whichever occurs first.

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Previous interventions as of 20/02/2024:

Arm A: Dose-escalation cohorts:
Participants will receive cevostamab SC, with step-up dosing on Days 1 and 8 of Cycle 1 (the duration of each cycle is 28 days) and then at the target dose on Day 15 in Cycle 1. From Cycle 2 onwards participants will receive cevostamab at the target dose, subcutaneously every 2 weeks

(Q2W) on Days 1 and 15 in Cycles 2 to 6, and every 4 weeks (Q4W) on Day 1 from Cycles 7 up to a maximum of 13 cycles, or until disease progression, or unacceptable toxicity, whichever occurs first.

Arm A: Dose-expansion cohorts:
Participants will receive cevostamab SC at the Maximum Tolerated Dose (MTD)/Recommended Phase 2 Dose (RP2D) determined from the Dose Escalation phase as per the schedule selected by the sponsor.

Arm B: Dose-escalation cohorts:
Participants will receive cevostamab SC, with step-up dosing on Days 1 and 4 of Cycle 1 followed by the target dose on Day 8. From Cycles 2-17 participants will receive cevostamab at the target dose, subcutaneously every 3 weeks (Q3W).

Arm B: Dose-expansion cohorts:
Participants will receive cevostamab SC at the MTD/RP2D determined from the Dose Escalation phase as per the schedule selected by the sponsor.

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Previous interventions:

Dose-escalation cohorts:
Participants will receive cevostamab SC, with step-up dosing on Days 1 and 8 of Cycle 1 (the duration of each cycle is 28 days) and then at the target dose on Day 15 in Cycle 1. From Cycle 2 onwards participants will receive cevostamab at the target dose, subcutaneously every 2 weeks (Q2W) on Days 1 and 15 in Cycles 2 to 6, and every 4 weeks (Q4W) on Day 1 from Cycles 7 up to a maximum of 13 cycles, or until disease progression, or unacceptable toxicity, whichever occurs first.

Dose-expansion cohorts:
Participants will receive cevostamab SC at the Maximum Tolerated Dose (MTD)/Recommended Phase 2 Dose (RP2D) determined from the Dose Escalation phase as per the schedule selected by the sponsor.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Cevostamab

Primary outcome(s)
Current primary outcome measure as of 09/06/2025:
1. Percentage of participants with adverse events (AEs) from screening up to 90 days after the end of treatment (up to approximately 4 years 1 month)
2. Percentage of participants with severity of AEs determined according to National Cancer Institute-Common Terminology Criteria for Adverse Events Version 5.0 (NCI CTCAE v5.0) and American Society of Transplantation and Cellular Therapy (ASTCT) Consensus Grading for CRS

from screening up to 90 days after the end of treatment (up to approximately 4 years 1 month)
3. Recommended Phase II Dose (RP2D) of SC cevostamab that is safe and tolerable and measured using DLT in cycle 1 (up to 28 days)

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Previous primary outcome measure as of 20/02/2024:

1. Percentage of participants with adverse events (AEs) from screening up to 90 days after the end of treatment (up to approximately 4 years 1 month)
2. Percentage of participants with severity of adverse events determined according to National Cancer Institute-Common Terminology Criteria for Adverse Events Version 5.0 (NCI CTCAE v5.0) and American Society of Transplantation and Cellular Therapy (ASTCT) Consensus Grading for Cytokine Release Syndrome (CRS) from screening up to 90 days after the end of treatment (up to approximately 4 years 1 month)
3. Recommended Phase II Dose (RP2D) of SC cevostamab that is safe and tolerable and measured using Dose Limiting Toxicity (DLT) in cycle 1 (28 days)

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Previous primary outcome measure:

1. Percentage of participants with adverse events (AEs) from screening up to 30 days after the end of treatment (up to approximately 2 years)
2. Percentage of participants with severity of adverse events determined according to National Cancer Institute-Common Terminology Criteria for Adverse Events Version 5.0 (NCI CTCAE v5.0) and American Society of Transplantation and Cellular Therapy (ASTCT) Consensus Grading for Cytokine Release Syndrome (CRS) from screening up to 30 days after the end of treatment (up to approximately 2 years)
3. Recommended Phase II Dose (RP2D) of SC cevostamab that is safe and tolerable and measured using Dose Limiting Toxicity (DLT) in cycle 1 (28 days)

Key secondary outcome(s))

Current secondary outcome measures as of 09/09/2025:
1. Objective response rate (ORR) is defined as the percentage of participants with a stringent complete response (sCR), complete response (CR), very good partial response (VGPR), or partial response (PR) on two consecutive occasions as determined by the investigator according to International Myeloma Working Group (IMWG) Uniform Response Criteria measured from baseline up to end of treatment (up to approximately 4 years 1 month)
2. Percentage of participants with CR/sCR from baseline up to end of treatment (up to approximately 4 years 1 month)
3. Percentage of participants with VGPR from baseline up to end of treatment (up to approximately 4 years 1 month)
4. Progression-free survival (PFS) as determined by the investigator according to IMWG Uniform Response Criteria from the time of enrollment to the first occurrence of disease progression or death from any cause, whichever occurs first (up to approximately 4 years 1 month)
5. Duration of response (DOR) as determined by the investigator according to IMWG Uniform Response Criteria measured from the date of first documented response of PR or better until date of disease progression or death from any cause (up to approximately 4 years 1 month)
6. Time to first response as determined by the investigator according to IMWG Uniform Response Criteria measured from the time of initiation of study treatment to achieving a confirmed PR or better (up to approximately 4 years 1 month)

7. Time to best response as determined by the investigator according to IMWG Uniform Response Criteria measured from the time of initiation of study treatment to achieving the deepest response (up to approximately 4 years 1 month)
8. Overall survival (OS) as determined by the investigator according to IMWG Uniform Response Criteria measured from the time of initiation of study treatment to death from any cause (up to approximately 4 years 1 month)
9. Serum concentration of cevostamab measured using validated ELISA at multiple timepoints from Cycle 1 (each cycle is of 28 days) Day 1 up to Cycle 13 Day 3 and end of treatment visit (up to approximately 4 years 1 month)
10. Area under the concentration-time curve (AUC) of cevostamab measured using non-compartmental analysis or population pharmacokinetic (PK) modelling approach as appropriate at multiple time points from Cycle 1 (each cycle is of 28 days) Day 1 up to Cycle 13 Day 3 and end of treatment visit (up to approximately 4 years 1 month)
11. Maximum observed serum concentration (Cmax) of cevostamab measured using non-compartmental analysis or population PK modelling approach as appropriate at multiple time points from Cycle 1 (each cycle is of 28 days) Day 1 up to Cycle 13 Day 3 and end of treatment visit (up to approximately 4 years 1 month)
12. Minimum observed serum concentration (Cmin) of cevostamab measured using non-compartmental analysis or population PK modelling approach as appropriate at multiple time points from Cycle 1 (each cycle is of 28 days) Day 1 up to Cycle 13 Day 3 and end of treatment visit (up to approximately 4 years 1 month)
13. Clearance (CL/F) of cevostamab measured using non-compartmental analysis or population PK modelling approach as appropriate at multiple time points from Cycle 1 (each cycle is of 28 days) Day 1 up to Cycle 13 Day 3 and end of treatment visit (up to approximately 4 years 1 month)
14. Volume of distribution at steady state measured by non-compartmental analysis or population PK modelling approach as appropriate at multiple time points from Cycle 1 (each cycle is of 28 days) Day 1 up to Cycle 13 Day 3 and end of treatment visit (up to approximately 4 years 1 month)
15. Number of participants with anti-drug antibody (ADA) using a titered approach including screening, confirmatory, titering, and neutralizing assays (screening, confirmatory and titering assays are validated ELISAs; neutralizing assay is a validated cell-based assay) at baseline and during the study (up to approximately 4 years 1 month)

Previous secondary outcome measures as of 20/02/2024:

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date of disease progression or death from any cause (up to approximately 4 years 1 month)
6. Time to first response as determined by the investigator according to IMWG Uniform Response Criteria measured from the time of initiation of study treatment to achieving a confirmed PR or better (up to approximately 4 years 1 month)
7. Time to best response as determined by the investigator according to IMWG Uniform Response Criteria measured from the time of initiation of study treatment to achieving the deepest response (up to approximately 4 years 1 month)
8. Minimal residual disease (MRD) negativity as defined by next-generation sequencing (NGS) (< 10-5) on bone marrow aspirate prior to initiation of study treatment (screening), at Cycle 2 (each cycle is of 28 days) Day 1 (within 3 days prior to dosing) and when needed to confirm response (up to approximately 4 years 1 month)
9. Overall survival (OS) as determined by the investigator according to IMWG Uniform Response Criteria measured from the time of initiation of study treatment to death from any cause (up to approximately 4 years 1 month)
10. Serum concentration of cevostamab measured using validated ELISA at multiple timepoints from Cycle 1 (each cycle is of 28 days) Day 1 up to Cycle 13 Day 3 and end of treatment visit (up to approximately 4 years 1 month)
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15. Volume of distribution at steady state measured non-compartmental analysis or population PK modelling approach as appropriate at multiple time points from Cycle 1 (each cycle is of 28 days) Day 1 up to Cycle 13 Day 3 and end of treatment visit (up to approximately 4 years 1 month)
16. Number of participants with anti-drug antibody (ADA) using a titered approach including screening, confirmatory, titering, and neutralizing assays (screening, confirmatory and titering assays are validated ELISAs; neutralizing assay is a validated cell-based assay) at baseline and during the study (up to approximately 4 years 1 month)

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Previous secondary outcome measures:

1. Objective response rate (ORR) is defined as the percentage of participants with a stringent complete response (sCR), complete response (CR), very good partial response (VGPR), or partial response (PR) on two consecutive occasions as determined by the investigator according to International Myeloma Working Group (IMWG) Uniform Response Criteria measured from baseline up to end of treatment (up to approximately 2 years)
2. Percentage of participants with CR/sCR from baseline up to end of treatment (up to

approximately 2 years)
3. Percentage of participants with VGPR from baseline up to end of treatment (up to approximately 2 years)
4. Progression-free survival (PFS) as determined by the investigator according to IMWG Uniform Response Criteria from the time of enrollment to the first occurrence of disease progression or death from any cause, whichever occurs first (up to approximately 2 years)
5. Duration of response (DOR) as determined by the investigator according to IMWG Uniform Response Criteria measured from the date of first documented response of PR or better until date of disease progression or death from any cause (up to approximately 2 years)
6. Time to first response as determined by the investigator according to IMWG Uniform Response Criteria measured from the time of initiation of study treatment to achieving a confirmed PR or better (up to approximately 2 years)
7. Time to best response as determined by the investigator according to IMWG Uniform Response Criteria measured from the time of initiation of study treatment to achieving the deepest response (up to approximately 2 years)
8. Minimal residual disease (MRD) negativity as defined by next-generation sequencing (NGS) (< 10-5) on bone marrow aspirate prior to initiation of study treatment (screening), at Cycle 2 (each cycle is of 28 days) Day 1 (within 3 days prior to dosing) and when needed to confirm response (up to approximately 2 years)
9. Overall survival (OS) as determined by the investigator according to IMWG Uniform Response Criteria measured from the time of initiation of study treatment to death from any cause (up to approximately 2 years)
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16. Number of participants with anti-drug antibody (ADA) using a titered approach including screening, confirmatory, titering, and neutralizing assays (screening, confirmatory and titering assays are validated ELISAs; neutralizing assay is a validated cell-based assay) at baseline and during the study (up to approximately 2 years)

Completion date
30/11/2026

Eligibility

Key inclusion criteria
1. Age ≥18 years at time of signing Informed Consent Form
2. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1
3. Life expectancy of at least 12 weeks
4. Participants with a diagnosis of R/R MM for which no established therapy for multiple myeloma (MM) is appropriate and available, or intolerance to those established therapies
5. Agreement to provide bone marrow biopsy and aspirate samples
6. Adverse events from prior anti-cancer therapy resolved to Grade less than or equal to (≤) 1, except any grade alopecia and peripheral sensory or motor neuropathy which must have resolved to Grade ≤ 2
7. Measurable disease defined by laboratory test results

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Current participant exclusion criteria as of 06/06/2024:
1. Prior treatment with cevostamab or another agent targeting fragment crystallizable receptor-like 5 (FcRH5)
2. Inability to comply with protocol-mandated hospitalization and activities restrictions
3. 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)
4. Prior use of any monoclonal antibody, radioimmunoconjugate, or antibody-drug conjugate as anti-cancer therapy within 4 weeks prior to first study treatment, except for the use of non-myeloma therapy
5. Prior treatment with systemic checkpoint inhibitors, including, but not limited to anti-cytotoxic T-lymphocyte associated (CTLA4), anti-programmed death-1 (PD-1), and anti-programmed death-ligand 1 (PD-L1) therapeutic antibodies within 12 weeks or 5 half-lives of the drug, whichever is shorter, prior to first study treatment
6. Prior treatment with allogeneic or autologous chimeric antigen receptor (CAR) T-cell therapy within 12 weeks prior to first study treatment
7. Known treatment-related, immune-mediated adverse events associated with prior checkpoint inhibitors
8. Known history of hemophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS)

9. 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
10. Treatment with radiotherapy within 4 weeks (systemic radiation) or 14 days (focal radiation) prior to first study treatment
11. Autologous stem cell transplant (SCT) within 100 days prior to first study treatment
12. Prior allogeneic SCT
13. Prior solid organ transplantation
14. Circulating plasma cell count exceeding 500/microlitres (μL) or 5% of the peripheral blood white cells
15. History of autoimmune disease
16. History of confirmed progressive multifocal leukoencephalopathy
17. History of severe allergic or anaphylactic reactions to monoclonal antibody therapy (or recombinant antibody-related fusion proteins)
18. Known history of amyloidosis (e.g., positive Congo Red stain or equivalent in tissue biopsy)
19. Participants with lesions in proximity of vital organs that may develop sudden decompensation/deterioration in the setting of a tumor flare
20. History of other malignancy within 2 years prior to screening, except those with negligible risk of metastasis or death
21. Current or past history of central nervous system (CNS) disease, such as stroke, epilepsy, CNS vasculitis, neurodegenerative disease, or CNS involvement by MM
22. Significant cardiovascular disease that may limit a participant's ability to adequately respond to a CRS event
23. Symptomatic active pulmonary disease or requiring supplemental oxygen
24. Known active bacterial, viral, fungal, mycobacterial, parasitic, or other infection (excluding fungal infections of nail beds) at study enrollment, or any major episode of infection requiring treatment with IV antimicrobials where the last dose of IV antimicrobial was given within 14 days prior to first study treatment
25. 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. 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
26. Positive and quantifiable Epstein-Barr virus (EBV) polymerase chain reaction (PCR), or cytomegalovirus (CMV) PCR prior to start of study treatment
27. Known or suspected chronic active EBV infection
28. Recent major surgery within 4 weeks prior to first study treatment
29. Positive serologic or PCR test results for acute or chronic Hepatitis B virus (HBV) infection
30. Acute or chronic Hepatitis C virus (HCV) infection
31. Known history of Human Immunodeficiency Virus (HIV) seropositivity
32. Administration of a live, attenuated vaccine within 4 weeks prior to first study treatment or anticipation that such a live attenuated vaccine will be required during the study
33. Treatment with systemic immunosuppressive medications (including, but not limited to, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor agents), with the exception of corticosteroid treatment ≤ 10 mg/day prednisone or equivalent within 2 weeks prior to first study treatment
34. History of illicit drug or alcohol abuse within 12 months prior to screening, in the investigator’ s judgment
35. Any medical condition or abnormality in clinical laboratory tests that, in the investigator’s judgement, precludes the patient’s safe participation in and completion of the study, or which could affect compliance with the protocol or interpretation of results

Previous participant exclusion criteria as of 20/02/2024 to 06/06/2024:
1. Prior treatment with cevostamab or another agent targeting fragment crystallizable receptor-like 5 (FcRH5)
2. Inability to comply with protocol-mandated hospitalization and activities restrictions
3. Pregnant or breastfeeding, or intending to become pregnant during the study or within 3 months after the last dose of study drug
4. Prior use of any monoclonal antibody, radioimmunoconjugate, or antibody-drug conjugate as anti-cancer therapy within 4 weeks prior to first study treatment, except for the use of non-myeloma therapy
5. Prior treatment with systemic checkpoint inhibitors, including, but not limited to anti-CTLA4, anti-PD-1, and anti-PD-L1 therapeutic antibodies within 12 weeks or 5 half-lives of the drug, whichever is shorter, prior to first study treatment
6. Prior treatment with allogeneic or autologous chimeric antigen receptor (CAR) T-cell therapy within 12 weeks prior to first study treatment
7. Known treatment-related, immune-mediated adverse events associated with prior checkpoint inhibitors
8. Known history of hemophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS)
9. 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
10. Treatment with radiotherapy within 4 weeks (systemic radiation) or 14 days (focal radiation) prior to first study treatment
11. Autologous stem cell transplant (SCT) within 100 days prior to first study treatment
12. Prior allogeneic SCT
13. Prior solid organ transplantation
14. Circulating plasma cell count exceeding 500/microlitres (µL) or 5% of the peripheral blood white cells
15. History of autoimmune disease
16. History of confirmed progressive multifocal leukoencephalopathy
17. History of severe allergic or anaphylactic reactions to monoclonal antibody therapy (or recombinant antibody-related fusion proteins)
18. Known history of amyloidosis (e.g., positive Congo Red stain or equivalent in tissue biopsy)
19. Participants with lesions in proximity of vital organs that may develop sudden decompensation/deterioration in the setting of a tumor flare
20. History of other malignancy within 2 years prior to screening, except those with negligible risk of metastasis or death
21. Current or past history of central nervous system (CNS) disease, such as stroke, epilepsy, CNS vasculitis, neurodegenerative disease, or CNS involvement by MM
22. Significant cardiovascular disease that may limit a participant's ability to adequately respond to a CRS event
23. Symptomatic active pulmonary disease or requiring supplemental oxygen
24. Known active bacterial, viral, fungal, mycobacterial, parasitic, or other infection (excluding fungal infections of nail beds) at study enrollment, or any major episode of infection requiring treatment with IV antimicrobials where the last dose of IV antimicrobial was given within 14 days prior to first study treatment
25. 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. 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
26. Positive and quantifiable Epstein-Barr virus (EBV) PCR, or CMV PCR prior to start of study treatment

27. Known or suspected chronic active Epstein-Barr virus (EBV) infection
28. Recent major surgery within 4 weeks prior to first study treatment
29. Positive serologic or polymerase chain reaction (PCR) test results for acute or chronic Hepatitis B virus (HBV) infection
30. Acute or chronic Hepatitis C virus (HCV) infection
31. Known history of Human Immunodeficiency Virus (HIV) seropositivity
32. Administration of a live, attenuated vaccine within 4 weeks prior to first study treatment or anticipation that such a live attenuated vaccine will be required during the study
33. Treatment with systemic immunosuppressive medications (including, but not limited to, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor agents), with the exception of corticosteroid treatment ≤ 10 mg/day prednisone or equivalent within 2 weeks prior to first study treatment
34. History of illicit drug or alcohol abuse within 12 months prior to screening, in the investigator' s judgment
35. Any medical condition or abnormality in clinical laboratory tests that, in the investigator's judgement, precludes the patient's safe participation in and completion of the study, or which could affect compliance with the protocol or interpretation of results

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Previous participant exclusion criteria as of 10/03/2023:
1. Inability to comply with protocol-mandated hospitalization and activities restrictions
2. Pregnant or breastfeeding, or intending to become pregnant during the study or within 3 months after the last dose of study drug
3. Prior use of any monoclonal antibody, radioimmunoconjugate, or antibody-drug conjugate as anti-cancer therapy within 4 weeks prior to first study treatment, except for the use of non-myeloma therapy
4. Prior treatment with systemic checkpoint inhibitors, including, but not limited to anti-CTLA4, anti-PD-1, and anti-PD-L1 therapeutic antibodies within 12 weeks or 5 half-lives of the drug, whichever is shorter, prior to first study treatment
5. Prior treatment with allogeneic or autologous chimeric antigen receptor (CAR) T-cell therapy within 12 weeks prior to first study treatment
6. Known treatment-related, immune-mediated adverse events associated with prior checkpoint inhibitors
7. 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
8. Treatment with radiotherapy within 4 weeks (systemic radiation) or 14 days (focal radiation) prior to first study treatment
9. Autologous stem cell transplant (SCT) within 100 days prior to first study treatment
10. Prior allogeneic SCT
11. Prior solid organ transplantation
12. Circulating plasma cell count exceeding 500/microlitres (μL) or 5% of the peripheral blood white cells
13. History of autoimmune disease
14. History of confirmed progressive multifocal leukoencephalopathy
15. History of severe allergic or anaphylactic reactions to monoclonal antibody therapy (or recombinant antibody-related fusion proteins)
16. Known history of amyloidosis (e.g., positive Congo Red stain or equivalent in tissue biopsy)
17. Participants with lesions in proximity of vital organs that may develop sudden decompensation/deterioration in the setting of a tumor flare
18. History of other malignancy within 2 years prior to screening, except those with negligible

risk of metastasis or death
19. Current or past history of central nervous system (CNS) disease, such as stroke, epilepsy, CNS vasculitis, neurodegenerative disease, or CNS involvement by MM
20. Significant cardiovascular disease that may limit a participant's ability to adequately respond to a CRS event
21. Symptomatic active pulmonary disease or requiring supplemental oxygen
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31. Any medical condition or abnormality in clinical laboratory tests that, in the investigator's judgement, precludes the patient's safe participation in and completion of the study, or which could affect compliance with the protocol or interpretation of results

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4. Prior treatment with systemic checkpoint inhibitors, including, but not limited to anti-CTLA4, anti-PD-1, and anti-PD-L1 therapeutic antibodies within 12 weeks or 5 half-lives of the drug, whichever is shorter, prior to first study treatment
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7. 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
8. Treatment with radiotherapy within 4 weeks (systemic radiation) or 14 days (focal radiation) prior to first study treatment
9. Autologous stem cell transplant (SCT) within 100 days prior to first study treatment
10. Prior allogeneic SCT or solid organ transplantation

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12. History of autoimmune disease
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23. Known history of Human Immunodeficiency Virus (HIV) seropositivity

Date of first enrolment
13/01/2022

Date of final enrolment
31/10/2025

Locations

Countries of recruitment
Australia

Belgium

Greece

Italy

Korea, South

Study participating centre
Royal Adelaide Hospital
Haematology Clinical Trials
Adelaide
Australia
5000

Study participating centre

University of Athens Medical School - Regional General Hospital Alexandra
Athens
Greece
115 28

Study participating centre
Evangelismos General Hospital of Athens
Athens
Greece
106 76

Study participating centre
St Vincent's Hospital Melbourne
Fitzroy
Victoria
Australia
3065

Study participating centre
Istituto Clinico Humanitas
Rozzano (MI)
Lombardia
Italy
20089

Study participating centre
Royal Prince Alfred Hospital
Camperdown
New South Wales
Australia
2050

Study participating centre
Seoul National U. Hospital imCORE
Seoul
Korea, South
110744

Study participating centre

Asan Medical Center – PPDS
Seoul
Korea, South
05505

Study participating centre
UZ Brussel
Brussel
Belgium
1090

Study participating centre
Azienda Ospedaliero Universitaria di Bologna Policlinico S.Orsola-Malpighi
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Emilia-Romagna
Italy
40138

Sponsor information

Organisation
Genentech Inc.

Funder(s)

Funder type
Industry

Funder Name
Genentech

Alternative Name(s)
Genentech, Inc., Genentech USA, Inc., Genentech USA

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to participant-level data not being a regulatory requirement

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes