# 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	<b>Recruitment status</b> Recruiting	[X] Prospectively registered [_] Protocol
Registration date 08/12/2021	<b>Overall study status</b> Ongoing	<ul> <li>Statistical analysis plan</li> <li>Results</li> </ul>
Last Edited 09/06/2025	<b>Condition category</b> Cancer	<ul><li>Individual participant data</li><li>[X] Record updated in last year</li></ul>

### 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

To identify the best dose of cevostamab SC for the next phase (Phase II) of the study
 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 injectionrelated 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

#### **Study website** https://forpatients.roche.com/en/trials/cancer/multiple-myeloma/study-evaluating-the-safetyand-activity-of-cevostamab--bfcr4350.html

# **Contact information**

**Type(s)** Public

**Contact name** Dr Clinical Trials

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# Additional identifiers

EudraCT/CTIS number Nil known

# **IRAS number**

**ClinicalTrials.gov number** Nil known

**Secondary identifying numbers** 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

### Secondary study design

Non randomised study

Study setting(s) Other

**Study type(s)** Treatment

**Participant information sheet** No participant information sheet available

### 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.

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.

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

Pharmaceutical study type(s)

Pharmacokinetic, Safety and activity

### Phase

Phase I

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

Cevostamab

### Primary outcome measure

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)

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)

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)

### Secondary outcome measures

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 noncompartmental 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 noncompartmental 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 noncompartmental 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:

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. 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)

11. Area under the concentration-time curve (AUC) of cevostamab measured using noncompartmental 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)

12. Maximum observed serum concentration (Cmax) of cevostamab measured using noncompartmental 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)

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14. 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)

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)

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)

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 2 years)

11. Area under the concentration-time curve (AUC) of cevostamab measured using noncompartmental 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 2 years)

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# Overall study start date

12/05/2021

# 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 ( $\leq$ ) 1, except any grade alopecia and peripheral sensory or motor neuropathy which must have resolved to Grade  $\leq$  2

7. Measurable disease defined by laboratory test results

# Participant type(s)

Patient

#### **Age group** Adult

**Lower age limit** 18 Years

Sex

Both

**Target number of participants** 110

### Key exclusion criteria

Current participant exclusion criteria as of 06/06/2024:

1. Prior treatment with cevostamab or another agent targeting fragment crystallizable receptorlike 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 nonmyeloma therapy

5. Prior treatment with systemic checkpoint inhibitors, including, but not limited to anticytotoxic 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 receptorlike 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 ( $\mu$ L) 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

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

Previous participant exclusion criteria as of 10/03/2023:

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

22. 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 antibiotics where the last dose of IV antibiotics was given within 14 days prior to first study treatment

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Previous exclusion criteria:

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8. Treatment with radiotherapy within 4 weeks (systemic radiation) or 14 days (focal radiation) prior to first study treatment

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22. Acute or chronic Hepatitis C virus (HCV) infection

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** Bologna Emilia-Romagna Italy 40138

# Sponsor information

**Organisation** Genentech Inc.

**Sponsor details** 

Building 1 Grenzacherstrasse 124 Basel Switzerland CH-4058 +41 616878333 global.trial\_information@roche.com

Sponsor type

Industry

Website https://www.roche.com/about/

# Funder(s)

Funder type Industry

**Funder Name** Genentech

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

**Funding Body Type** Private sector organisation

**Funding Body Subtype** For-profit companies (industry)

**Location** United States of America

# **Results and Publications**

**Publication and dissemination plan** Planned publication in a high-impact peer-reviewed journal

Intention to publish date 30/11/2027

#### 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