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A study to evaluate safety, pharmacokinetics, and activity of cevostamab in patients with relapsed or refractory multiple myeloma

Submission date 04/03/2022	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 09/05/2022	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 08/01/2025	**Condition category** Cancer	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
Multiple myeloma (MM) is a malignant disease that remains incurable despite advances in treatment, with an average survival of 8-10 years and 2-3 years for high-risk disease. Increased survival has been achieved with the introduction of new treatments.

Nevertheless, despite this clear progress, most patients eventually relapse, and the outcome of patients after they become refractory, or ineligible to receive further treatment, is quite poor, with survival of approx 1 year. Therefore, relapsed or refractory (R/R) MM continues to be a significant unmet medical need, and novel therapeutic agents are still necessary.

This study is testing a drug called cevostamab given by itself, or in combination with pomalidomide plus dexamethasone, or with daratumumab plus dexamethasone.

Initial clinical data indicates that cevostamab monotherapy is of benefit to heavily pretreated patients with R/R MM. Combination with additional myeloma agents offers the potential to further improve outcome.

The purpose of this study is to test cevostamab administered using a different dosing schedule than studied in previous clinical trials and cevostamab in combination with pomalidomide plus dexamethasone and with daratumumab plus dexamethasone to find out if they are safe and to understand the way the body processes the drugs.

Cevostamab is an experimental drug, which means health authorities have not approved cevostamab for the treatment of MM. Pomalidomide, daratumumab, and dexamethasone are all approved for use in MM.

Who can participate?
Adults over 18 years, with MM.

What does the study involve?
Total time in the study will depend on how the individual tolerates study treatment as well as how their MM responds to the treatment. This could range from 1 day to 12 months or longer. There will be approximately 6 patients recruited at 2 UK sites. 120 patients in total will be recruited worldwide.

What are the possible benefits and risks of participating?
Benefits:
The participant's health may or may not improve in this study, but the information that is learned may help other people who have a similar medical condition in the future.

Risks:
There are risks, discomforts, and inconveniences associated with any research study. It is possible that these general risks could be increased by the addition of test medications. Some of the general risks may be potentially life threatening and may not have been previously reported.

Study Assessment Risks:
Some of these procedures take place more often than they would if patients were not taking part in this study.

Radiation Exposure Risks:
The ionising/radioactive radiation in this study has undergone CRE/MPE review.

Blood Collection:
Taking blood samples may cause bruising and discomfort and a risk of infection or blood clots at the site of the blood collection. If patients have a central line, this may be used for blood samples. There is always a risk of infection at the site where the line is fitted.

Study Treatment:
The Study Drugs (cevostamab, pomalidomide, daratumumab, dexamethasone, and tocilizumab) will be given in a clinic with emergency equipment and staff who are trained to monitor for and respond to any potential medical emergencies.

Risks Associated with the Study Drugs:
Side effects can be referred to in the main PISICF due to the character count limit.

Unknown Risks:
It is possible that side-effects of the Study Drugs which are unknown at this time may occur during the study. Any new information that may affect participants' health or which may make the participants want to stop taking part in the study will be shared with them as soon as it becomes available.

Pregnancy Prevention:
There may be a risk in exposing an unborn child to study drugs, and all risks are not known at this time. Women must take precautions to avoid exposing an unborn child to study drugs, as described in the PIS-ICF.

Where is the study run from?
Not provided at time of registration

When is the study starting and how long is it expected to run for?
February 2022 to October 2024

Who is funding the study?
F.Hoffmann La Roche (Germany)

Who is the main contact?
Dr Rakesh Popat, rakesh.popat@ucl.ac.uk

Study website
https://forpatients.roche.com/en/trials/cancer/multiple-myeloma/a-study-evaluating-the-safety--pharmacokinetics--and-ac-86713.html

Contact information

Type(s)
Scientific

Contact name
Dr Aidan Cunningham

Contact details
Clinical Operations Lead
Roche Products Limited
6 Falcon Way, Shire Park
Welwyn Garden City
United Kingdom
AL7 1TW
+44 1707 384 115
welwyn.uk_ethics@roche.com

Type(s)
Principal Investigator

Contact name
Dr Rakesh Popat

Contact details
250 Euston Road
London
United Kingdom
NW1 2PG
-
rakesh.popat@ucl.ac.uk

Additional identifiers

EudraCT/CTIS number
2021-000238-33

IRAS number
1004618

ClinicalTrials.gov number
NCT04910568

Secondary identifying numbers
GO42552, IRAS 1004618, CPMS 51355

Study information

Scientific Title
An open-label, multicenter, phase Ib trial evaluating the safety, pharmacokinetics, and activity of cevostamab in patients with relapsed or refactory multiple myeloma (CAMMA 1)

Acronym
CAMMA 1

Study objectives
• To evaluate the safety and tolerability of single agent cevostamab in the modified weekly schedule
• To evaluate the safety and tolerability of cevostamab plus pomalidomide and dexamethasone (Pd)
• To evaluate the safety and tolerability of cevostamab plus daratumumab and dexamethasone (Dd)

• To make a preliminary assessment of the activity of single agent cevostamab in the modified weekly schedule
• To make a preliminary assessment of the activity of cevostamab plus Pd
• To make a preliminary assessment of the activity of cevostamab plus Dd
• To characterize the pharmacokinetics of cevostamab when given as a single agent and when given in combination with Pd and with Dd
• To confirm the exposures of pomalidomide and daratumumab when administered in combination with cevostamab
• To evaluate the immune response to cevostamab when given as a single agent and when given in combination with Pd and with Dd

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/05/2022, London Bridge Research Ethics Committee (2nd Floor, 2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)2071048387, +44 (0)207 104 8140, +44 (0)207 104 8016; londonbridge.rec@hra.nhs.uk), ref: 22/LO/0225

Study design
Interventional non randomized

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Multiple myeloma is a cancer that affects a type of white blood cell. Refractory means your cancer doesn't improve with treatment, or it stops responding to treatment.

Interventions
There are 3 treatment groups on this study:
Cevostamab monotherapy (Group A)
Cevostamab plus pomalidomide and dexamethasone (Group B)
Cevostamab plus daratumumab and dexamethasone (Group C)

The dose of cevostomab will start at a smaller dose and increase to a larger final dose. This is called the ‘target dose’ and the method of increasing the dose is called ‘step-up’.

Participants will be assigned to one of the availabel treatment groups by the medical monitor. This decision will be based on which treatment groups a participant can take part in and which treatment groups are open at the time.

In Group A, participants will receive Cevostamab only. Cevostamab will be administered in 28 day cycles as an injection into a vein in an arm, and this is expected to take approximately 4 hours.
In Group B, participants will receive a combination of Cevostamab and Pomalidomide.
Cevostamab will be administered in 28 day cycles as an injection into a vein in an arm, and this is expected to take approximately 4 hours.
Pomalidomide is a tablet that you swallow.

In Group C, participants will receive a combination of Cevostamab and Daratumumab.
Cevostamab will be administered in 21 day cycles as an injection into a vein in an arm, and this is expected to take approximately 4 hours.
Daratumumab is an injection under the skin in your abdomen.

In all groups participants will also receive Dexamethasone - this may be as a tablet to swallow, or as an injection into a vein in an arm.

Participants will be required to stay in hospital for observation at least 48 hours after each dose of the first 3 doses of Cevostamab so they can be closely monitored for possible side effects. One potential side effect is an infusion related reaction also known as Cytokine Release Syndrome (CRS).
If required this can be treated with Tocilizumab, which will be administered as an injection into a vein in an arm, and is expected to take approximately 1 hour.

The number of treatment cycles the participant receives, will depend on how they tolerate the study treatment, and how well their multiple myeloma responds to the treatment.

Once participants have stopped taking the study drug, they will be asked to come to the hospital for follow-up appointments, every 3 months. Participants may be contacted by telephone if unable to come to the hospital.

Intervention Type
Drug

Pharmaceutical study type(s)
Not Applicable

Phase
Phase I

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

Primary outcome measure
Incidence and severity of adverse events, with severity determined according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v5.0 and American Society of Transplantation and Cellular Therapy (ASTCT) Consensus Grading for Cytokine Release Syndrome up to approximately 3 years

Secondary outcome measures
Up to approximately 3 years:
1. Objective response rate (ORR)
2. Complete response (CR)/stringent complete response (sCR) rate
3. Rate of very good partial response (VGPR) or better
4. Progression-free survival (PFS)
5. Duration of response (DOR)
6. Time to first response
7. Time to best response
8. Minimal residual disease (MRD) negativity as defined by next-generation sequencing (NGS) on bone marrow aspirate
9. Overall survival (OS)

Arm A: Days (D) 1, 2, 3, 8, 9, 10, 15, 22 of Cycle (C) 1 (Single Step-Up) or D1, 2, 3, 8, 9, 10, 15, 16, 17, 22 of C1 (Double Step-Up); D1, 8, 15, 22 of C2; D1 and 15 of C3-6; D1 of C7-13; end of treatment; Arm B: D1, 2, 3, 8, 9, 10, 15, 16, 17 of Cevostamab Pre-Phase (CPP); D1, 15 of C1-6; D1 of C7 onwards; end of treatment; Arm C: D1, 2, 3, 4, 9, 10, 11, 16, 17, 18 of C1; D1 of C2; D 1, 8, 15 of C3; D1 of C4 onwards; end of treatment:
10. Serum concentration of cevostamab at specified timepoints
11. Pharmacokinetic (PK) parameters of cevostamab
12. Serum concentrations of pomalidomide and daratumumab at specified timepoints

Arm A: D1, 15 of C1-2; D1 for C3-13; end of treatment; Arm B: D1, 15 of CPP, C1; D1 of C2 onwards; end of treatment; Arm C: D2, 16 of C1; D1 of C2 onwards; end of treatment:
13. Prevalence of anti-drug antibodies (ADAs) against cevostamab at baseline and incidence of ADAs against cevostamab during the study

Overall study start date
26/02/2022

Completion date
01/10/2026

Eligibility

Key inclusion criteria
1. Age >= 18 years
2. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1
3. Life expectancy of at least 12 weeks
4. Agreement to undergo scheduled assessments and procedures including bone marrow biopsy and aspirate samples
5. Resolution of adverse events from prior anti-cancer therapy to Grade <=1
6. Measurable disease
7. Adequate hepatic and hematologic function
8. For women of childbearing potential: agreement to remain abstinent or use contraception, during the treatment period (including treatment interruptions) and for at least 2 months after the last dose of cevostamab and at least 3 months after the last dose of tocilizumab was administered
9. 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 cevostamab or tocilizumab was administered to avoid exposing the embryo and sexual partner

Additional Arm A-Specific Inclusion Criteria
10. 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
11. For Cohort B1S: Patients with R/R MM who have received at least 2 prior lines of treatment
12. For Cohort B1E: Patients with R/R MM who have received at least 1 prior line of treatment
13. Agreement to comply with all local requirements of the pomalidomide pregnancy risk minimization plan
14. Agreement to avoid donating blood during the treatment period and for at least 4 weeks after the last dose of pomalidomide
15. 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
16. 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, and agreement to refrain from donating sperm during this same period

Additional Arm C-Specific Inclusion Criteria
17. For Cohort C1S: Patients with R/R MM who have received at least 2 prior lines of treatment
18. For Cohort C1E: Patients with R/R MM who have received at least 1 prior line of therapy
19. For women of childbearing potential: agreement to remain abstinent or use contraceptive methods during the treatment period and for at least 3 months after the last dose of daratumumab was administered
20. For men: agreement to remain abstinent or use a condom during the treatment period and for at least 3 months after the last dose of daratumumab was administered to avoid exposing the embryo, and agreement to refrain from donating sperm during this same period

Participant type(s)

Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
120

Total final enrolment
126

Key exclusion criteria
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 2 months after the last dose of cevostamab or within 3 months after the last dose of tocilizumab
4. Prior use of any monoclonal antibody, radioimmunoconjugate, or antibody-drug conjugate as anti-cancer therapy within 4 weeks before first study treatment
5. Prior treatment with systemic immunotherapeutic agents within 12 weeks or 5 half-lives of the drug before first study treatment
6. Prior treatment with chimeric antigen receptor T (CAR T) cell therapy within 12 weeks before first study treatment
7. Known treatment-related, immune-mediated adverse events associated with prior checkpoint inhibitors
8. Treatment with radiotherapy within 4 weeks (systemic radiation) or 14 days (focal radiation) prior to first study treatment
9. Treatment with any chemotherapeutic agent or other anti-cancer agent within 4 weeks or 5 half-lives of the drug before first study treatment
10. Autologous stem cell transplant (SCT) within 100 days prior to first study treatment
11. Prior allogeneic SCT
12. Circulating plasma cell count exceeding 500/microliter or 5% of the peripheral blood white cells
13. Prior solid organ transplantation
14. History of autoimmune disease
15. History of confirmed progressive multifocal leukoencephalopathy
16. History of severe allergic or anaphylactic reactions to monoclonal antibody therapy
17. Known history of amyloidosis
18. Lesions in proximity of vital organs that may develop sudden decompensation/deterioration in the setting of a tumor flare
19. History of other malignancy within 2 years prior to screening
20. Current or past history of central nervous system (CNS) disease
21. Significant cardiovascular disease
22. Known history of Grade >=3 cytokine release syndrome (CRS) or immune effector cell associated neurotoxicity syndrome (ICANS) with prior bispecific therapies

23. Symptomatic active pulmonary disease or requiring supplemental oxygen
24. Known active bacterial, viral, fungal, mycobacterial, parasitic, or other infection
25. Known or suspected chronic active Epstein-Barr virus (EBV) infection
26. Recent major surgery within 4 weeks prior to first study treatment
27. Positive serologic or PCR test results for acute or chronic HBV infection
28. Acute or chronic hepatitis C virus (HCV) infection
29. Known history of HIV seropositivity
30. Administration of a live, attenuated vaccine within 4 weeks before first study treatment
31. Treatment with systemic immunosuppressive medications within 2 weeks prior to first study treatment
32. History of illicit drug or alcohol abuse within 12 months prior to screening
33. Any medical condition or abnormality in clinical laboratory tests that, in 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 the results

Additional Arm B-Specific Exclusion Criteria
34. Pregnant or breastfeeding, or intending to become pregnant 4 weeks prior to initiation of study treatment, during the study, or within 4 weeks after the last dose of pomalidomide
35. History of erythema multiforme, Grade >=3 rash, blistering, or severe hypersensitivity to prior treatment with immunomodulatory drugs such as thalidomide, lenalidomide, or pomalidomide
36. Inability to tolerate thromboprophylaxis, or contraindication to thromboprophylaxis
37. GI disease that might significantly alter absorption of oral drugs

Additional Arm C-Specific Exclusion Criteria
38. Pregnant or breastfeeding, or intending to become pregnant during the study or within 3 months after the last dose of daratumumab
39. Known hypersensitivity to biopharmaceuticals produced in CHO cells or any component of daratumumab formulations
40. Known chronic obstructive pulmonary disease (COPD) with a forced expiratory volume in 1 second (FEV1) <50% of predicted normal
41. Known moderate or severe persistent asthma within the past 2 years, or current uncontrolled asthma of any classification

Date of first enrolment
25/07/2021

Date of final enrolment
04/12/2024

Locations

Countries of recruitment
Australia

Canada

Denmark

England

France

Israel

Poland

Russian Federation

Spain

United Kingdom

Study participating centre
NIHR University College London Hospitals Clinical Research Facility
University College London Hospitals NHS Foundation Trust
4th Floor
170 Tottenham Court Road
London
United Kingdom
W1T 7HA

Study participating centre
NIHR Royal Marsden Clinical Research Facility
Fulham Road
London
United Kingdom
SW3 6JJ

Sponsor information

Organisation
Genentech Inc. c/o F.Hoffman-La Roche Ltd

Sponsor details
Grenzacherstrasse 124
Basel
Germany
4070
-
global.rochegenentechtrials@roche.com

Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
F.Hoffmann La Roche

Results and Publications

Publication and dissemination plan
Peer-reviewed scientific journals
Internal report
Conference presentation
Publication on website
Other
Roche has a Data Sharing Policy, which allows participants to request and receive global clinical study reports (CSRs) and other summary reports. Roche provides details of all its clinical trials on public websites: http://www.ClinicalTrials.gov, https://www.clinicaltrialsregister.eu
These websites can also be found at https://www.roche-trials.com
Links to these websites are provided to participants in the Participant Information Sheets.

Intention to publish date
01/10/2026

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No