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A platform trial investigating new combinations of therapies in patients with relapsed multiple myeloma

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Registration date 07/01/2021	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 06/01/2026	**Condition category** Cancer	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims

ProMMise is a study for patients with relapsed multiple myeloma (MM). Relapsed means it has returned after treatment. MM is rare, but the number of people living with it is increasing. Currently it is incurable. However, new treatments mean more people are surviving for longer, and around one-third of patients are now living for 10 years after diagnosis.

Although survival has improved, new treatments are required to extend life expectancy still further and to provide new options for hard-to-treat patients. Belantamab mafodotin (known as belamaf) is a new drug that attacks myeloma cells. Initial trials have shown a good response; on average the disease didn't return (progress) for 12 months. This was in a group of patients with refractory MM, meaning myeloma had returned after various treatments.

The aim of this study is to investigate the outcomes, safety, and tolerability of belamaf, both alone and in combination with standard-of-care myeloma agents, in relapsed refractory MM patients.

Who can participate?

Adult patients with a confirmed diagnosis of Multiple Myeloma who meet the inclusion criteria and do not meet any of the exclusion criteria.

What does the study involve?

This is a platform study, which means there will be several arms each looking at different treatment combinations. This will start with 2 or 3 trial arms, with other arms added later. The first arm will use belamaf alone. More arms will be added to look at belamaf used in combination with known myeloma drugs. The design means arms can be added easily as new combinations become available.

This study has two phases, which will take place sequentially for each arm. Participants will take part in one of these only. The first phase is focused on safety, providing close monitoring to check the doses of the drugs are safe and side effects are tolerable. There will then be an expansion phase, which will give researchers an indication of how effective the drugs are.

Trial Arm D involves a treatment combination that has already been investigated in another trial and focuses on the eye assessments required to treat with belamaf safely.

What are the possible benefits and risks of participating?
Belamaf is well tolerated. The main side effects are blurred vision and a reduced number of platelets in the blood (thrombocytopenia). Both of these effects resolve if treatment is paused, and in most cases treatment could continue.
Due to the new way belamaf works and its as yet limited identified side effects, combining this with existing myeloma drugs has the potential to improve the outlook for patients.

Where is the study run from?
University of Leeds (UK)

When is the study starting and how long is it expected to run for?
September 2019 to December 2030

Who is funding the study?
GlaxoSmithKline (UK)

Who is the main contact?
Mrs Heena Patel, ProMMise@leeds.ac.uk

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-belantamab-mafodotin-to-improve-treatment-for-myeloma-prommise

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2020-004058-31

Integrated Research Application System (IRAS)
1003553

Protocol serial number

HM20/134457

Study information

Scientific Title
A platform trial for relapsed patients to evaluate ongoing novel therapies in multiple myeloma in combination with standard of care therapies

Acronym
ProMMise

Study objectives
To investigate the outcomes, safety, and tolerability of the agent belantamab mafodotin, as both a monotherapy and in combination with standard of care myeloma agents, in relapsed refractory multiple myeloma patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/07/2021, West of Scotland REC 1 (West of Scotland Research Ethics Service, Admin Building, Level 2, Gartnavel Royal Hospital, 1055 Great Western Road, Glasgow, G12 0XH, United Kingdom; N/A; ggc.wosrec1@nhs.scot), ref: 21/WS/0065

Study design
Multi-centre multi-arm Phase I platform study, designed with the flexibility to open and close arms at different times

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Current interventions as of 04/02/2025:
This is a multi-centre, multi-arm, phase I platform study in relapsed/refractory multiple myeloma patients with 1-4 prior lines of therapy. The trial includes multiple treatment arms investigating different novel combinations of belamaf plus treatment(s). This may comprise of a dose escalation and dose expansion phase, or may use a previously approved recommended dose level. These trial arms have the flexibility to open or close depending on the stage of the trial, allowing continuous recruitment. Participants will remain on treatment until progression, withdrawal, or unacceptable toxicities.

A number of baseline assessments need to be conducted prior to the first administration of trial treatment. These include: Physical exam including height, weight, and Eastern Cooperative Oncology Group (ECOG) Performance Status, Charlson Comorbidity Index (CCI), haematology

and biochemistry assessments, urinalysis, PET-CT scan, electrocardiogram (ECG), ophthalmological examination, pregnancy test (if applicable), and Myeloma-Specific Quality of Life Questionnaire (MyPOS).

For trial arms (Arm-B) where the treatment combinations have never previously been used in this population of multiple myeloma patients, a dose escalation phase is required. A modified toxicity probability interval (mTPI-2) approach is proposed for dose-finding/safety evaluation, within each combination arm, to determine a safe dose schedule. The mTPI-2 is an adaptive model-based Bayesian design determining the probability that a patient experiences a DLT for each dose level given the observed data. Cohorts of 3 evaluable participants will be sequentially recruited to the combination arms of the trial until the recommended dose (RD) has been identified, or the trial stopped due to excessive toxicity at the lowest dose schedule. The dose schedule given to a subsequent cohort will be evaluated after all participants have been followed up for 1 cycle or experienced a DLT. The SRC will be presented with a complete safety report in addition to a set of predetermined dosing recommendations, such that all relevant information available may be considered before deciding upon the next dose schedule to be allocated.

Once safety has been confirmed, a dose-expansion phase is planned to assess the longer-term tolerability profile of the combination at the Recommended Dose. Patients will receive treatment in 28-day cycles until disease progression, withdrawal, or unacceptable toxicities.

Trial Arm D uses a combination which has already demonstrated a significant improvement in progression-free survival compared to standard-of-care treatment. Therefore, the trial design for Arm D does not include a dose escalation phase. Arm D uses a two-stage design to investigate if an alternative approach to ocular toxicity assessment using a clinician-led questionnaire called the Vision Related Anamnestic Tool (VRAT) can be used to safely guide belamaf dosing.

Participants will be allocated to an arm depending on which arms are open to recruitment. In order to allow assessment of the DLT period, arms will temporarily close during the dose-finding phase. Allocation to arms in the dose-escalation phase will be prioritised over the monotherapy arm and/or arms in the expansion phase. If multiple combination arms are open in the escalation stage, then prioritisation will be given to the cohort open the longest. If a participant is eligible for multiple arms in the expansion phase and all arms have a similar number of participants already allocated to them, then the participants will be allocated to one of the arms with equal probability. If there develops an imbalance between the arms (defined by a difference greater than a fixed constant in the number of participants allocated to each arm) then the procedure will skew the allocation in favour of those arms with fewer participants recruited.

Endpoint data will be collected at regular intervals during treatment and follow-up throughout the trial. This will be achieved by conducting the following trial procedures: physical examinations, ECOG, VRAT/ophthalmology assessments, pregnancy tests (if applicable), MyPOS questionnaire, Peripheral Blood Mononuclear Cell (PBMC) blood samples, and blood panels (chemistry & haematology).

Once the treatment phase is complete, participants will be followed up until one of the following occurs: disease progression, withdrawal, or unacceptable toxicities.

It is estimated patient may remain in treatment for approximately 1-3 years depending on response.

Previous interventions:
This is a multi-centre, multi-arm, phase I platform study in relapsed/refractory multiple myeloma patients with 1-3 prior lines of therapy. The study comprises a dose escalation phase and a dose expansion phase. The trial will investigate the safety of belamaf both as a monotherapy (once every 28-day treatment cycle, intravenously) and in novel combinations with other agents (belamaf once every other 28-day treatment cycle; combination treatments may vary). Participants will remain on treatment until progression, withdrawal, or unacceptable toxicities.

A number of baseline assessments need to be conducted prior to the first administration of trial treatment. These include: Physical exam including height, weight, and Eastern Cooperative Oncology Group (ECOG) Performance Status, haematology and biochemistry assessments, urinalysis, PET-CT scan, electrocardiogram (ECG), ophthalmological examination, pregnancy test (if applicable), and Myeloma-Specific Quality of Life Questionnaire (MyPOS).

As these treatment combinations have never previously been used in this population of multiple myeloma patients, a dose escalation phase is required for each combination arm. A monotherapy arm will be incorporated into the dose expansion phase to ensure the safety, toxicity, and efficacy data in the combination arms are interpretable within the context of the current study and patient population. A modified toxicity probability interval (mTPI-2) approach is proposed for dose-finding/safety evaluation, within each combination arm, to determine a safe dose schedule. The mTPI-2 is an adaptive model-based Bayesian design determining the probability that a patient experiences a DLT for each dose level given the observed data. Cohorts of 3 evaluable participants will be sequentially recruited to the combination arms of the trial until the recommended dose (RD) has been identified, or the trial stopped due to excessive toxicity at the lowest dose schedule. The dose schedule given to a subsequent cohort will be evaluated after all participants have been followed up for 1 cycle or experienced a DLT. The SRC will be presented with a complete safety report in addition to a set of predetermined dosing recommendations, such that all relevant information available may be considered before deciding upon the next dose schedule to be allocated.

Once safety has been confirmed, a dose-expansion phase is planned to assess the longer-term tolerability profile of the combination at the Recommended Dose. Patients will receive treatment in 28-day cycles until disease progression, withdrawal, or unacceptable toxicities.

Participants will be allocated to an arm depending on which arms are open to recruitment. In order to allow assessment of the DLT period, arms will temporarily close during the dose-finding phase. Allocation to arms in the dose-escalation phase will be prioritised over the monotherapy arm and/or arms in the expansion phase. If multiple combination arms are open in the escalation stage, then prioritisation will be given to the cohort open the longest. If a participant is eligible for multiple arms in the expansion phase and all arms have a similar number of participants already allocated them, then the participants will be allocated to one of the arms with equal probability. If there develops an imbalance between the arms (defined by a difference greater than a fixed constant in the number of participants allocated to each arm) then the procedure will skew the allocation in favour of those arms with fewer participants recruited.

Endpoint data will be collected at regular intervals during treatment and follow-up throughout the trial. This will be achieved by conducting the following trial procedures: physical examinations, ECOG, ophthalmology assessments, pregnancy tests (if applicable), MyPOS questionnaire, Peripheral Blood Mononuclear Cell (PBMC) blood samples, and blood panels (chemistry & haematology).

Once the treatment phase is complete, participants will be followed-up until one of the following occurs: disease progression, withdrawal, or unacceptable toxicities.

It is estimated patient may remain in treatment between approximately 1-3 years dependent on response.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Belantamab mafodotin

Primary outcome(s)
Dose finding phase:
1. Dose limiting toxicities within the first cycle of treatment measured using measured using adverse event collection and safety assessments between 0 and 28 days

Expansion phase:
1. Participant response assessed using the proportion of participants achieving at least a very good partial response (VGPR) whilst on trial treatment using International Myeloma Working Group (IMWG) criteria at the beginning of each cycle up from baseline until disease progression or stopping
2. Safety and toxicity measured using adverse events, graded using the Common Terminology Criteria for Adverse Events (CTCAE version 5.0), Serious Adverse Events (SAEs), Serious Adverse Reactions (SARs), and Serious Unexpected Serious Adverse Reactions (SUSARs), and determined by routine assessments at each site from 0 days until disease progression or stopping

Key secondary outcome(s))
1. Overall response rate measured from response assessments, using IMWG criteria, at the beginning of each cycle up from baseline until disease progression or stopping
2. MRD negativity rate measured using IMWG criteria from bone marrow samples taken at 6, 12 and 18 months
3. Progression-free survival measured as the time from registration to first documented evidence of disease progression or death, where response is measured at the beginning of each cycle and diseases progression
4. Maximum response measured from response assessments, using IMWG criteria, at the beginning of each cycle up from baseline until disease progression or stopping
5. Time to maximum response measured from response assessments, using IMWG criteria, at the beginning of each cycle from baseline up until disease progression
6. Duration of response measured from response assessments, using IMWG criteria, at the beginning of each cycle from baseline up until disease progression
7. Compliance to therapy measured using dosing information (such as dose omission, delays, modifications) reported after each cycle of treatment from baseline until disease progression or stopping
8. Quality of life measured using the Myeloma-Specific Quality of Life Questionnaire (MyPOS) at baseline, once every 3 cycles during treatment (starting at C3D1), at end of treatment, and then during post-treatment follow-up at each ophthalmology appointment the participant undergoes for eye toxicity

Completion date
31/12/2030

Eligibility

Key inclusion criteria
Current inclusion criteria as of 04/02/2025:
1. Histologically or cytologically confirmed diagnosis of multiple myeloma (MM) as defined according to International Myeloma Working Group (IMWG) criteria
2. Relapsed or refractory disease, having received between 1 and 3 prior lines of therapy which include a proteasome inhibitor (including bortezomib, carfilzomib, ixazomib) and an immunomodulatory imide drug (including thalidomide, lenalidomide, pomalidomide).
3. Have measurable disease with at least one of the following:
- Paraprotein ≥5 g/l
- Serum free light chains ≥100 mg/l with abnormal ratio for light chain only myeloma
- Bence Jones protein ≥ 200 mg/day
OR
- Non-secretory/ Oligosecretory disease defined within this protocol as ≥30% neoplastic plasma cells in the bone marrow
4. Aged ≥18 years on day of signing informed consent
5. Not pregnant or breastfeeding, and one of the following conditions applies:
5.1. Not a woman of childbearing potential (WOCBP)
5.2. Is a WOCBP and all of the following apply:
5.2.1. Is using a highly effective (with a failure rate of <1% per year) method of contraception (preferably with low user dependency) from 4 weeks prior to the start of treatment, during the intervention period, and for the contraceptive time frame specified in the arm-specific eligibility criteria.
5.2.2. Have a negative urine or serum pregnancy test as outlined in each treatment sub-protocol and agree to use a highly effective method of contraception from 4 weeks prior to the start of treatment, during the study, and for 9 months after the last dose of belamaf
5.2.3. Have agreed not to donate eggs (ova, oocytes) for the purpose of reproduction during this period
6. Male participants of childbearing potential who agree to one of the following from the time of dosing on C1D1 until 6 months after the last dose of study treatment, to allow for clearance of any altered sperm:
6.1. Abstinence from heterosexual intercourse as their preferred and usual lifestyle (abstinent on a long-term and persistent basis), or agree to use a male condom (even if they have undergone a successful vasectomy)
6.2. If applicable, WOCBP (including pregnant females) partners to use an additional highly effective contraceptive method with a failure rate of <1% per year
6.3 Refrain from donating sperm during this period
7. Agree to refrain from donating blood while on trial drug, including during dose interruptions and for 120 days after discontinuation from this trial
8. All prior treatment-related toxicities (defined by National Cancer Institute- Common Toxicity Criteria for Adverse Events (NCI-CTCAE), version 4.03), except for alopecia, must be ≤Grade 1 at the time of enrolment
9. Adequate organ function as defined by the following assessments:
- Absolute neutrophil count (ANC) ≥1 X 109/L
- Haemoglobin ≥80 g/l
- Platelets ≥75 x10^9/l
- Total bilirubin ≤1.5 x ULN

- ALT ≤2.5 x ULN
10. Calculated creatinine clearance ≥40 ml/min/1.73 m² using Cockcroft-Gault formula
11. Spot urine <500 mg/g
12. ECOG Performance Status between grade 0-2

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Previous inclusion criteria as of 07/11/2023:
1. Histologically or cytologically confirmed diagnosis of multiple myeloma (MM) as defined according to International Myeloma Working Group (IMWG) criteria
2. Relapsed or refractory disease, having received between 1 and 3 prior lines of therapy which include a proteasome inhibitor (including bortezomib, carfilzomib, ixazomib) and an immunomodulatory imide drug (including thalidomide, lenalidomide, pomalidomide).
3. Have measurable disease with at least one of the following:
3.1. Paraprotein ≥5 g/l
3.2. Serum free light chains ≥100 mg/l with abnormal ratio for light chain only myeloma
3.3. Bence Jones protein ≥ 200 mg/day
4. Aged ≥18 years on day of signing informed consent
5. Not pregnant or breastfeeding, and one of the following conditions applies:
5.1. Not a woman of childbearing potential (WOCBP)
5.2. Is a WOCBP and all of the following apply:
5.2.1. Is using a highly effective (with a failure rate of <1% per year) method of contraception (preferably with low user dependency) from 4 weeks prior to the start of treatment, during the intervention period, and for the contraceptive time frame specified in the arm specific eligibility criteria.
5.2.2. Have a negative urine or serum pregnancy test as outlined in each treatment sub-protocol and agree to use a highly effective method of contraception from 4 weeks prior to the start of treatment, during the study, and for 9 months after the last dose of belamaf
5.2.3. Have agreed not to donate eggs (ova, oocytes) for the purpose of reproduction during this period
6. Male participants of childbearing potential who agree to one of the following from the time of dosing on C1D1 until 6 months after the last dose of study treatment, to allow for clearance of any altered sperm:
6.1. Abstinence from heterosexual intercourse as their preferred and usual lifestyle (abstinent on a long term and persistent basis), or agree to use a male condom (even if they have undergone a successful vasectomy)
6.2. If applicable, WOCBP (including pregnant females) partners to use an additional highly effective contraceptive method with a failure rate of <1% per year
6.3 Refrain from donating sperm during this period
7. Agree to refrain from donating blood while on trial drug, including during dose interruptions and for 120 days after discontinuation from this trial
8. All prior treatment-related toxicities (defined by National Cancer Institute- Common Toxicity Criteria for Adverse Events (NCI-CTCAE), version 4.03), except for alopecia, must be ≤Grade 1 at the time of enrolment
9. Adequate organ function as defined by the following assessments:
9.1. Absolute neutrophil count (ANC) ≥1 X 109/L
9.2. Haemoglobin ≥80 g/l
9.3. Platelets ≥75 x10⁹/l
9.4. Total bilirubin ≤1.5 x ULN
9.5. ALT ≤2.5 x ULN
10. Calculated creatinine clearance ≥40 ml/min/1.73 m² using Cockcroft-Gault formula
11. Spot urine <500 mg/g

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Original inclusion criteria:
1. Histologically or cytologically confirmed diagnosis of multiple myeloma (MM) as defined according to International Myeloma Working Group (IMWG) criteria
2. Relapsed or refractory disease, having received between 1 and 3 prior lines of therapy which include a proteasome inhibitor (including bortezomib, carfilzomib, ixazomib) and an immunomodulatory imide drug (including thalidomide, lenalidomide, pomalidomide).
3. Have measurable disease with at least one of the following:
3.1. Paraprotein ≥5 g/l
3.2. Serum free light chains ≥100 mg/l with abnormal ratio for light chain only myeloma
3.3. Bence Jones protein ≥ 200 mg/day
4. Aged ≥18 years on day of signing informed consent
5. Not pregnant or breastfeeding, and one of the following conditions applies:
5.1. Not a woman of childbearing potential (WOCBP)
5.2. Is a WOCBP and all of the following apply:
5.2.1. Is using a highly effective (with a failure rate of <1% per year) method of contraception (preferably with low user dependency)
5.2.2. Have a negative urine or serum pregnancy test as outlined in each treatment sub-protocol and agree to use a highly effective method of contraception from 4 weeks prior to the start of treatment, during the study, and for 9 months after the last dose of belamaf
5.2.3. Have agreed not to donate eggs (ova, oocytes) for the purpose of reproduction during this period
6. Male participants of childbearing potential who agree to one of the following from the time of dosing on C1D1 until 6 months after the last dose of study treatment, to allow for clearance of any altered sperm:
6.1. Abstinence from heterosexual intercourse as their preferred and usual lifestyle (abstinent on a long term and persistent basis), or agree to use a male condom (even if they have undergone a successful vasectomy)
6.2. If applicable, WOCBP (including pregnant females) partners to use an additional highly effective contraceptive method with a failure rate of <1% per year
6.3 Refrain from donating sperm during this period
7. Agree to refrain from donating blood while on trial drug, including during dose interruptions and for 120 days after discontinuation from this trial
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9. Adequate organ function as defined by the following assessments:
9.1. Absolute neutrophil count (ANC) ≥1 X 109/L
9.2. Haemoglobin ≥80 g/l
9.3. Platelets ≥75 x10^9/l
9.4. Total bilirubin ≤1.5 x ULN
9.5. ALT ≤2.5 x ULN
10. Calculated creatinine clearance ≥40 ml/min/1.73 m^2 using Cockcroft-Gault formula
11. Spot urine <500 mg/g

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
110 years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current exclusion criteria as of 04/02/2025:
1. Non-measurable disease (does not meet Inclusion Criteria 3), solitary bone or solitary extramedullary plasmacytoma, plasma cell leukaemia, POEMS syndrome (plasma cell dyscrasia with polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes), systemic amyloidosis
2. Currently participating and receiving trial therapy or has participated in a trial of an investigational agent and received trial therapy or used an investigational device within 28 days prior to dose allocation
3. Any of the following prior treatments:
3.1. Autologous stem cell transplantation <3 months prior to dose allocation
3.2. Anti-cancer monoclonal antibody (mAb) within 14 days prior to dose allocation or who has not recovered (≤Grade 1 or at baseline) from adverse events due to agents administered more than 4 weeks earlier ≤Grade 2 neuropathy with no pain is an exception to this criterion.
3.3. Chemotherapy, targeted small molecule therapy, or therapeutic radiation therapy within 14 days prior to dose allocation or who has not recovered (≤Grade 1 or at baseline) from adverse events due to a previously administered agent. ≤Grade 2 neuropathy with no pain is an exception to this criterion. Palliative radiotherapy for pain control and bisphosphonates is permitted
3.4. Treatment with plasmapheresis within 4 weeks prior to dose allocation (Palliative radiotherapy for pain control and bisphosphonates is permitted. Corticosteroids for myeloma disease control are permitted up to 7 days prior to first dose.)
4. Significant cardiac disease as determined by the investigator including:
4.1. Known or suspected cardiac amyloidosis
4.2. Congestive heart failure of Class III or IV of the New York Heart Association (NYHA) classification
4.3. Uncontrolled angina, hypertension, or arrhythmia
4.4. History of myocardial infarction, acute coronary syndromes (including unstable angina), coronary angioplasty, or stenting or bypass grafting in the past 3 months prior to dose allocation
4.5. Uncontrolled or severe cardiovascular disease including uncontrolled hypertension, clinically significant uncontrolled and/or untreated arrhythmias, ECG abnormalities such as second-degree (Mobitz Type II) or third-degree atrioventricular block Corrected QT interval (QTcF) >530 msec based on average value of triplicate ECGs performed within 14 days of registration
5. Prior treatment with a B-cell maturation antigen (BCMA) targeted therapy
6. Current corneal epithelial disease except for mild changes in corneal epithelium

7. Requirement to wear contact lenses
8. Active renal condition (infection, requirement for dialysis, or any other condition that could affect participant's safety) or unstable liver or biliary disease (defined by the presence of ascites, encephalopathy, coagulopathy, hypoalbuminemia, esophageal or gastric varices, persistent jaundice, or cirrhosis) per investigator assessment. Stable non-cirrhotic chronic liver disease (including Gilbert's syndrome or asymptomatic gallstones) or hepatobiliary involvement of malignancy is acceptable if otherwise meets entry criteria.
9. Known history of Human Immunodeficiency Virus (HIV)
10. Known active Hepatitis B or Hepatitis C confirmed by antibody test or RNA test within 3 months prior to dose allocation.
11. Any major surgery within 4 weeks prior to dose allocation.
12. Active infection requiring systemic antibiotic, antiviral, or antifungal treatment within 7 days of dose allocation.
13. Known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs chemically related to belamaf or any other components of the study treatment.
14. Planned for autologous or allogeneic stem cell transplant
15. Known additional malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin or squamous cell carcinoma of the skin that has undergone potentially curative therapy or in situ cervical cancer or carcinoma of the prostate undergoing surveillance.
16. Evidence of active mucosal or internal bleeding
17. Pregnancy or lactating
18. Any medical or psychiatric condition or substance abuse disorder which, in the opinion of the investigator, contraindicates the participant's eligibility for the trial, including a known intolerance to any of the trial treatments.
19. Has Grade >2 Neuropathy without pain or Grade >1 Neuropathy with pain.

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Previous exclusion criteria as of 07/11/2023:
1. Non-measurable disease, solitary bone or solitary extramedullary plasmacytoma, plasma cell leukaemia, POEMS syndrome (plasma cell dyscrasia with polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes), or systemic amyloidosis
2. Currently participating and receiving trial therapy or has participated in a trial of an investigational agent and received trial therapy or used an investigational device within 28 days prior to dose allocation
3. Any of the following prior treatments:
3.1. Autologous stem cell transplantation <3 months prior to dose allocation
3.2. Anti-cancer monoclonal antibody (mAb) within 14 days prior to dose allocation or who has not recovered (≤Grade 1 or at baseline) from adverse events due to agents administered more than 4 weeks earlier ≤Grade 2 neuropathy with no pain is an exception to this criterion.
3.3. Chemotherapy, targeted small molecule therapy, or therapeutic radiation therapy within 14 days prior to dose allocation or who has not recovered (≤Grade 1 or at baseline) from adverse events due to a previously administered agent. ≤Grade 2 neuropathy with no pain is an exception to this criterion. Palliative radiotherapy for pain control and bisphosphonates is permitted
3.4. Treatment with plasmapheresis within 4 weeks prior to dose allocation (Palliative radiotherapy for pain control and bisphosphonates is permitted. Corticosteroids for myeloma disease control are permitted up to 7 days prior to the 1st dose.)
4. Significant cardiac disease as determined by the investigator including:
4.1. Known or suspected cardiac amyloidosis
4.2. Congestive heart failure of Class III or IV of the New York Heart Association (NYHA)

classification
4.3. Uncontrolled angina, hypertension, or arrhythmia
4.4. History of myocardial infarction, acute coronary syndromes (including unstable angina), coronary angioplasty, or stenting or bypass grafting in the past 3 months prior to dose allocation
4.5. Uncontrolled or severe cardiovascular disease including uncontrolled hypertension, clinically significant uncontrolled and/or untreated arrhythmias, ECG abnormalities such as second-degree (Mobitz Type II) or third-degree atrioventricular block Corrected QT interval (QTcF) >530 msec based on average value of triplicate ECGs performed within 14 days of registration
5. Prior treatment with a B-cell maturation antigen (BCMA) targeted therapy
6. Current corneal epithelial disease except for mild changes in corneal epithelium
7. Requirement to wear contact lenses
8. Active renal condition (infection, requirement for dialysis, or any other condition that could affect participant's safety) or unstable liver or biliary disease (defined by the presence of ascites, encephalopathy, coagulopathy, hypoalbuminemia, esophageal or gastric varices, persistent jaundice, or cirrhosis) per investigator assessment. Stable non-cirrhotic chronic liver disease (including Gilbert's syndrome or asymptomatic gallstones) or hepatobiliary involvement of malignancy is acceptable if otherwise meets entry criteria.
9. Known history of Human Immunodeficiency Virus (HIV)
10. Known active Hepatitis B or Hepatitis C confirmed by antibody test or RNA test within 3 months prior to dose allocation.
11. Any major surgery within 4 weeks prior to dose allocation.
12. Active infection requiring systemic antibiotic, antiviral, or antifungal treatment within 7 days of dose allocation.
13. Known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs chemically related to belamaf or any other components of the study treatment.
14. Planned for autologous or allogeneic stem cell transplant
15. Known additional malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin or squamous cell carcinoma of the skin that has undergone potentially curative therapy or in situ cervical cancer or carcinoma of the prostate undergoing surveillance.
16. No evidence of active mucosal or internal bleeding
17. Not pregnant or lactating
18. Any medical or psychiatric condition or substance abuse disorder which, in the opinion of the investigator, contraindicates the participant's eligibility for the trial, including a known intolerance to any of the trial treatments.
19. Has Grade >2 Neuropathy without pain or Grade >1 Neuropathy with pain.

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Original exclusion criteria:
1. Non-measurable disease, solitary bone or solitary extramedullary plasmacytoma, plasma cell leukaemia, POEMS syndrome (plasma cell dyscrasia with polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes), or systemic amyloidosis
2. Currently participating and receiving trial therapy or has participated in a trial of an investigational agent and received trial therapy or used an investigational device within 28 days prior to the first dose of trial treatment
3. Any of the following prior treatments:
3.1. Autologous stem cell transplantation <3 months prior to the first dose of trial treatment
3.2. Anti-cancer monoclonal antibody (mAb) within 14 days prior to the first dose of trial treatment or who has not recovered (≤Grade 1 or at baseline) from adverse events due to agents administered more than 4 weeks earlier ≤Grade 2 neuropathy with no pain is an exception to this criterion.

3.3. Chemotherapy, targeted small molecule therapy, or therapeutic radiation therapy within 14 days prior to the first dose of trial treatment or who has not recovered (≤Grade 1 or at baseline) from adverse events due to a previously administered agent. ≤Grade 2 neuropathy with no pain is an exception to this criterion. Palliative radiotherapy for pain control and bisphosphonates is permitted
3.4. Treatment with plasmapheresis within 4 weeks prior to the first dose of trial treatment
4. Significant cardiac disease as determined by the investigator including:
4.1. Known or suspected cardiac amyloidosis
4.2. Congestive heart failure of Class III or IV of the New York Heart Association (NYHA) classification
4.3. Uncontrolled angina, hypertension, or arrhythmia
4.4. History of myocardial infarction, acute coronary syndromes (including unstable angina), coronary angioplasty, or stenting or bypass grafting in the past 3 months
e. Uncontrolled or severe cardiovascular disease including uncontrolled hypertension, clinically significant uncontrolled and/or untreated arrhythmias, ECG abnormalities such as second-degree (Mobitz Type II) or third-degree atrioventricular block
5. Corrected QT interval (QTcF) >530 msec based on average value of triplicate ECGs performed within 14 days of registration
6. Prior treatment with a B-cell maturation antigen (BCMA) targeted therapy
7. Current corneal epithelial disease except for mild changes in corneal epithelium
8. Requirement to wear contact lenses
9. Active renal condition (infection, requirement for dialysis, or any other condition that could affect participant's safety) or unstable liver or biliary disease (defined by the presence of ascites, encephalopathy, coagulopathy, hypoalbuminemia, esophageal or gastric varices, persistent jaundice, or cirrhosis) per investigator assessment. Stable non-cirrhotic chronic liver disease (including Gilbert's syndrome or asymptomatic gallstones) or hepatobiliary involvement of malignancy is acceptable if otherwise meets entry criteria.
10. Known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the trial
11. Known history of Human Immunodeficiency Virus (HIV)
12. Known active Hepatitis B or Hepatitis C confirmed by antibody test or RNA test within 3 months prior to the first dose of study treatment
13. Any major surgery within 4 weeks prior to registration
14. Active infection requiring systemic antibiotic, antiviral, or antifungal treatment within 7 days of treatment
15. Known immediate or delayed hypersensitivity reaction or idiosyncrasy to belamaf or drugs chemically related to it
16. Planned for autologous or allogeneic stem cell transplant
17. Systemic treatment within 14 days prior to the first dose with any of the following:
17.1. strong inhibitors of CYP1A2 (fluvoxamine, enoxacin, ciprofloxacin)
17.2. strong inhibitors of CYP3A (clarithromycin, telithromycin, itraconazole, voriconazole, ketoconazole, nefazodone, posaconazole)
17.3. strong CYP3A inducers (rifampin, rifapentine, rifabutin, carbamazepine, phenytoin, phenobarbital)
17.4. use of Ginkgo biloba or St. John's Wort.
18. Known additional malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin or squamous cell carcinoma of the skin that has undergone potentially curative therapy or in situ cervical cancer or carcinoma of the prostate undergoing surveillance.
19. No evidence of active mucosal or internal bleeding
20. Not pregnant or lactating

Date of first enrolment
11/05/2022

Date of final enrolment
30/06/2026

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre
University College London Hospitals
-
London
England
NW1 2BU

Study participating centre
Royal Marsden Hospital
-
London
England
SW3 6JJ

Study participating centre
Southampton General Hospital
-
Southampton
England
SO16 6YD

Study participating centre
Nottingham University Hospitals
-
Nottingham
England
NG7 2UH

Study participating centre
St James's University Hospital
Beckett Street
Leeds
England
LS9 7TF

Study participating centre
Cardiff and Vale NHS Trust
Cardigan House
University Hospital of Wales
Heath Park
Cardiff
Wales
CF14 4XW

Sponsor information

Organisation
University of Leeds

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
De-identified individual participant data datasets generated and/or analysed during the current study will be available upon request from the Clinical Trials Research Unit, University of Leeds (contact CTRU-DataAccess@leeds.ac.uk in the first instance). Data will be made available at the end of the trial, i.e. usually when all primary and secondary endpoints have been met and all key analyses are complete. Data will remain available from then on for as long as CTRU retains the data.

CTRU makes data available by a 'controlled access' approach. Data will only be released for legitimate secondary research purposes, where the Chief Investigator, Sponsor and CTRU agree that the proposed use has scientific value and will be carried out to a high standard (in terms of scientific rigour and information governance and security), and that there are resources available to satisfy the request. Data will only be released in line with participants' consent, all applicable laws relating to data protection and confidentiality, and any contractual obligations to which the CTRU is subject. No individual participant data will be released before an appropriate agreement is in place setting out the conditions of release. The agreement will govern data retention, usually stipulating that data recipients must delete their copy of the released data at the end of the planned project.

The CTRU encourages a collaborative approach to data sharing, and believes it is best practice for researchers who generated datasets to be involved in subsequent uses of those datasets. Recipients of trial data for secondary research will also receive data dictionaries, copies of key trial documents and any other information required to understand and reuse the released datasets.

The conditions of release for aggregate data may differ from those applying to individual participant data. Requests for aggregate data should also be sent to the above email address to discuss and agree suitable requirements for release.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes