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A Phase I/IIa trial of HMBD-001 in advanced HER3-positive solid tumours

Submission date
08/01/2026

Recruitment status
No longer recruiting

Registration date
25/06/2026

Overall study status
Completed

Last Edited
30/09/2026

Condition category
Cancer

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
This clinical trial is evaluating a drug called HMBD-001, a type of targeted cancer drug called a monoclonal antibody. It works by finding a protein on cancer cells called HER3, which is found in high numbers in some types of cancers including those that contain fusions in a gene called NRG1. By attaching itself to this HER3, it may then work to kill the cancer cells or to stop them from growing. The main aims are to find out the best dose of HMBD-001 that can be given to patients alone and in combination with other anti-cancer agents, more about the potential side effects of HMBD-001 and how they can be treated, and what happens to HMBD-001 inside the body and how it affects cancer cells.
Part A is a 'dose escalation' phase where small groups of patients will receive increasing doses of HMBD-001 on its own (as a single agent) to find the safest dose that best targets cancer cells.
Part B is a 'dose expansion' phase where larger groups of patients with specific cancer types that are known to have high levels of the protein HER3 or that have a confirmed NRG1 gene fusion will receive the highest doses of HMBD-001 considered to be safe as monotherapy from Part A in combination with other anti-cancer drugs that are already licensed for use.
In Part B Arm 1, patients will receive HMBD-001 in combination with enzalutamide. Enzalutamide is a drug used to treat prostate cancer. Prostate cancer is known to be sensitive to androgens (hormones associated with male characteristics), and enzalutamide blocks the action of androgens by limiting the binding of androgens to androgen receptors. This slows the growth of prostate cancer cells and may kill them.

Who can participate?
Part A: Patients aged 16 years and over with advanced solid tumours or with a NRG1 fusion rearrangement or HER amplification.
Part B: Patients aged 18 years and over with metastatic castration-resistant prostate cancer (mCRPC) confirmed as HER3 positive with no PTEN loss or with a NRG1 fusion rearrangement.

What does the study involve?
There are two parts to this trial, a dose escalation part and a dose expansion part.
In the dose escalation part of the trial, the first few patients joining have a low dose of HMBD-001. If they don't have any serious side effects, the next few patients have a higher dose. This process continues until the doctors find the best dose to give to patients to target cancer cells.

In the dose expansion part, patients with mCRPC will receive the highest dose of HMBD-001 considered to be safe found in Part A as well as enzalutamide.
Blood samples will be taken to find out what happens to HMBD-001 in the body and to check how HMBD-001 is working.

What are the possible benefits and risks of participating?
This is the first time that HMBD-001 is being used in humans. The possible direct benefit is that study drug may help treat the patient's cancer, although the chances of this are unknown. The trial may reveal information which may help improve the treatment for patients with cancer in the future.

The information we have on potential side effects is based on laboratory tests and experience with similar drugs which have been given to patients.

Possible side effects include:

• feeling or being sick
• diarrhoea
• changes to your heartbeat
• changes to the levels of magnesium or potassium in your blood
• a drop in red blood cells causing tiredness and breathlessness
• liver changes
• skin rash
• tiredness (fatigue)
• fertility problems

Where is the study run from?
Cancer Research UK

When is the study starting and how long is it expected to run for?
The trial started recruiting in November 2021 and completed in September 2025.

Who is funding the study?
Cancer Research UK

Who is the main contact?
Cancer Research UK Centre for Drug Development; drugdev@cancer.org.uk

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-hmbd-001-for-solid-cancers-that-have-spread

Contact information

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT05057013

Clinical Trials Information System (CTIS)
2020-005891-36

Integrated Research Application System (IRAS)
298897

Central Portfolio Management System (CPMS)
49816

Protocol serial number

CRUKD/22/002

Study information

Scientific Title
A Cancer Research UK Phase I/IIa open-label, dose escalation and expansion trial of HMBD-001 (an anti-HER3 monoclonal antibody) given intravenously as a single agent and in combination in patients with advanced HER3-positive solid tumours

Study objectives
Primary Objectives:
1. To propose a recommended dose and schedule for Phase II evaluation (RP2D) of HMBD-001 as a single agent
2. To establish the maximum tolerated dose or maximum administered dose of HMBD 001 in patients with advanced HER3 positive solid tumours
3. To assess the safety and tolerability profile of HMBD-001 in patients with advanced HER3 positive solid tumours
4. To establish a recommended dose and schedule of HMBD-001 to be given with the selected combination agent(s)
5. To assess the safety and tolerability profile of HMBD-001 in combination with selected agent (s) in the chosen expansion tumour types
6. To evaluate preliminary evidence of anti-tumour activity of HMBD-001 in combination in the chosen expansion tumour types

Secondary Objectives:
1. To evaluate the preliminary anti-tumour activity of HMBD-001 when given as a single agent
2. To characterise the pharmacokinetic (PK) profile or determine limited PK parameters of HMBD-001 when given as a single agent and in combination
3. To evaluate the preliminary anti-tumour activity of HMBD-001 when given as a single agent and in combination
4. To determine progression free survival and overall survival in the selected tumour types

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 09/09/2021, London Surrey Borders Research Ethics Committee (Skipton House, 80 London Road, London, SE1 6LH, United Kingdom; +44 020 7104 8104; Surreyborders.rec@hra.nhs.uk), ref: 21/LO/0477

Primary study design
Interventional

Allocation
Non-randomized controlled trial

Masking
Open (masking not used)

Control

Active

Assignment
Parallel

Purpose
Treatment

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Bladder Cancer
Triple Negative Breast Cancer
Castration-resistant Prostate Cancer (metastatic)
Cervical Cancer
RAS Wild Type Colorectal Cancer
Endometrial Cancer
Gastric Cancer
Hepatocellular Carcinoma
Melanoma
Non-small Cell Lung Cancer
Oesophageal Cancer
Ovarian Cancer
Pancreatic Cancer
Squamous Cell Cancers of the Head and Neck

Interventions
This is an open label, multi-centre, first in human, Phase I/IIa adaptive design trial with initial single patient intrapatient dose escalation followed by inter-patient dose escalation to determine the recommended Phase II dose (RP2D) of HMBD-001 as a single agent.

The clinical trial's two parts consist of: Part A (the dose escalation phase), and Part B (the dose expansion phase).

In Part A, patients with advanced solid tumours will receive HMBD-001 diluted in 0.9% sodium chloride, administered once a week as a 120-minute intravenous (IV) infusion. The starting dose will be 150 mg. Each cycle of HMBD-001 will consist of

28 days with no break in between and patients may continue for up to six cycles. If the patient is showing benefit, they may continue beyond six cycles.

In Part B, patients with metastatic castration-resistant prostate cancer (mCRPC) confirmed as HER3 positive with no PTEN loss or with a NRG1 fusion rearrangement will receive the HMBD-001 recommended Phase 2 dose (RP2D) as determined in Part A, diluted in 0.9% sodium chloride and administered once a week as a 120-minute IV infusion, in combination with enzalutamide administered at a fixed dose of 160 mg once daily, in 28-day cycles with no break between cycles. Prior to commencing combination therapy, patients may receive one 28-day cycle of enzalutamide monotherapy to confirm that their disease does not respond to enzalutamide alone. HMBD-001 may be administered for up to six cycles; enzalutamide may be continued until disease progression or unacceptable toxicity.

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
HMBD-001

Primary outcome(s)
1. Number of patients who experienced Dose Limiting Toxicities (DLTs) (Part A)
DLTs graded for severity using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version (v) 5.0, measured by count of patients per arm.
[Time Frame: From first dose onwards until completion of Cycle 1 (28 days)]

2. Number of patients who experienced DLTs (Part B Arm 1)
DLTs graded for severity using the NCI CTCAE v5.0, measured by count of patients per arm.
[Time Frame: From first dose of combination therapy onwards until completion of Cycle 1 (28 days)]

3. Number of adverse events (AEs) by arm considered to be at least possibly related to HMBD-001 (Part A and Part B Arm 1)
Number of AEs related to HMBD-001 given as a single agent and in combination with enzalutamide, graded according to NCI CTCAE v5.0.
[Time Frame: From the date of written informed consent until the end of the safety follow-up period (maximum [max] 42 weeks per patient)]

4. Number of Grade 3, 4 and 5 AEs by arm considered to be at least possibly related to HMBD-001 (Part A and Part B Arm 1)
Number of Grade 3, 4 and 5 AEs related to HMBD-001 given as a single agent and in combination with enzalutamide, graded according to NCI CTCAE v5.0.
[Time Frame: From the date of written informed consent until the end of the safety follow-up period (max 42 weeks per patient)]

5. Overall response rate (ORR) within six cycles of HMBD-001 (Part B Arm 1)
Proportion of patients who achieve a best response of complete response (CR) or partial response (PR), based on Response Evaluation Criteria in Solid Tumours (RECIST) v1.1 and/or Prostate Cancer Working Group 3 (PCWG3) Criteria as applicable, within six cycles of HMBD-001 in combination with enzalutamide.
[Time Frame: From baseline radiological disease assessment until 28 days after last dose of HMBD-001 (max 36 weeks per patient)]

Key secondary outcome(s)
1. ORR within six cycles of HMBD-001 (Part A)
Proportion of patients who achieve a best response of CR or PR, based on RECIST v1.1 and/or PCWG3 Criteria as applicable, within six cycles of HMBD-001 monotherapy.
[Time Frame: From baseline radiological disease assessment until 28 days after last dose of HMBD-001 (max 32 weeks per patient)]

2. Maximum observed serum concentration (Cmax) of HMBD-001 (Part A and Part B Arm 1)
Cmax of HMBD-001 in serum, analysed via enzyme linked immunosorbent assay (ELISA). Not all

patients will be analysed at all timepoints.
[Time Frame: Up to 31 timepoints from first dose until 28 days after the last dose of HMBD-001 (max 28 weeks per patient)]

3. Minimum observed serum concentration (Cmin) of HMBD-001 (Part A and Part B Arm 1)
Cmin of HMBD-001 in serum, analysed via ELISA. Not all patients will be analysed at all timepoints.
[Time Frame: Up to 31 timepoints from first dose until 28 days after the last dose of HMBD-001 (max 28 weeks per patient)]

4. Area under the serum concentration-time curve (AUC) of HMBD-001 (Part A and Part B Arm 1)
AUC of HMBD-001, analysed via ELISA. Not all patients will be analysed at all timepoints.
[Time Frame: Up to 31 timepoints from first dose until 28 days after the last dose of HMBD-001 (max 28 weeks per patient)]

5. Terminal elimination half-life (t½) of HMBD-001 (Part A and Part B Arm 1)
t½ of HMBD-001 in serum, analysed via ELISA. Not all patients will be analysed at all timepoints.
[Time Frame: Up to 31 timepoints from first dose until 28 days after the last dose of HMBD-001 (max 28 weeks per patient)]

6. Steady state volume of distribution of HMBD-001 in serum (Part A and Part B Arm 1)
Volume of distribution of HMBD-001 in serum at steady state, analysed via ELISA. Not all patients will be analysed at all timepoints.
[Time Frame: Up to 31 timepoints from first dose until 28 days after the last dose of HMBD-001 (max 28 weeks per patient)]

7. Total body clearance of HMBD-001 (Part A and Part B Arm 1)
Total body clearance of HMBD-001 measured in serum, analysed via ELISA. Not all patients will be analysed at all timepoints.
[Time Frame: Up to 31 timepoints from first dose until 28 days after the last dose of HMBD-001 (max 28 weeks per patient)]

8. ORR within 8 and 16 weeks of commencing HMBD-001 (Part A and Part B Arm 1)
Proportion of patients achieving a best response of CR or PR, according to RECIST v1.1 and/or PCWG3 Criteria as applicable, within 8 and 16 weeks of commencing HMBD-001 as monotherapy and in combination with enzalutamide.
[Time Frame: From baseline radiological disease assessment up to 16 weeks post first HMBD-001 administration (max 24 weeks per patient)]

9. Disease control rate within six cycles of HMBD-001 (Part A and Part B Arm 1)
Proportion of patients achieving a best response of CR, PR or stable disease (SD), based on RECIST v1.1 and/or PCWG3 Criteria as applicable, within six cycles of HMBD-001 as monotherapy and in combination with enzalutamide.
[Time Frame: From baseline radiological disease assessment up to 28 days post last HMBD-001 administration (max 36 weeks per patient)]

10. Duration of response (Part A and Part B Arm 1)
The median duration in days from the first observation of a CR or PR, according to RECIST v1.1 and/or PCWG3 Criteria as applicable, until either progressive disease (PD) or death from any cause, in patients with a confirmed CR or PR.
[Time Frame: From the date of first recorded response until 24 months after the last enrolled patient's first dose of HMBD-001 (max 48 months per patient)]

11. Duration of clinical benefit (Part A and Part B Arm 1)
The median duration in days from the first administration of HMBD-001 until either PD or death from any cause, in patients who achieve a CR, PR, or SD for at least 24 weeks, according to RECIST v1.1 and/or PCWG3 Criteria as applicable.
[Time Frame: From the date of first recorded response until 24 months after the last enrolled patient's first dose of HMBD-001(max 48 months per patient)]

12. Progression free survival (Part B Arm 1)
The median duration in days from first dose of HMBD-001 to death from any cause or PD according to RECIST v1.1 and/or PCWG3 Criteria as applicable.
[Time Frame: From first dose of HMBD-001 until 24 months after the last enrolled patient's first dose of HMBD-001 (max 48 months per patient)]

13. Overall survival (Part B Arm 1)
The median time from first dose of HMBD-001 to death from any cause.
[Time Frame: From first dose of HMBD-001 until 24 months after the last enrolled patient's first dose of HMBD-001 (max 48 months per patient)]

Completion date
10/09/2025

Eligibility

Key inclusion criteria
1. Written (signed and dated) informed consent and be capable of co-operating with HMBD-001 administration and follow-up.

2. Part A: Monotherapy Dose Escalation
Histologically confirmed advanced or metastatic solid tumours resistant or refractory to conventional treatment, or for which no conventional therapy exists or is not considered appropriate by the Investigator or is declined by the patient.
Patients with tumour types known to overexpress HER3 including:
• Bladder cancer
• Triple negative breast cancer
• Castration-resistant prostate cancer
• Cervical cancer
• RAS wild type colorectal cancer
• Endometrial cancer
• Gastric cancer
• Hepatocellular carcinoma
• Melanoma
• Non-small cell lung cancer
• Oesophageal cancer
• Ovarian cancer
• Pancreatic cancer
• Squamous cell cancers of the head and neck

Patients with a confirmed existing NRG1 fusion rearrangement or HER amplification will also be considered eligible.

Part B Arm 1: HMBD-001 and Enzalutamide Combination
• Histologically confirmed metastatic castration-resistant prostate adenocarcinoma without neuroendocrine differentiation or small-cell features
• Serum testosterone concentration ≤50 ng/dL sustained by medical or surgical castration
• Patients must have progressive disease prior to study enrolment.
• PSA at screening >1 ng/mL
• Confirmed high HER3 expression
• Absence of PTEN loss
• Patients with confirmed existing NRG1 fusion rearrangement will also be considered eligible.

3. Life expectancy of at least 12 weeks.
4. Eastern Cooperative Oncology Group performance status of 0 or 1.
5. Haematological and biochemical indices within the protocol specified ranges.
6. Patients with advanced prostate cancer must have castrate levels of testosterone and have received a next generation hormonal agent (at least one of abiraterone, enzalutamide, apalutamide or darolutamide).
7. Part A: Aged 16 years or over at the time consent is given.
8. Part B Arm 1: Aged 18 years or over at the time consent is given.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 Years

Upper age limit
110 Years

Sex
All

Total final enrolment
25

Key exclusion criteria
1. Radiotherapy (except for palliative reasons), chemotherapy, endocrine therapy (with the exceptions of life-long hormone suppression such as luteinising hormone-releasing hormone [LHRH] agents in prostate cancer and patients that are being re-screened for the trial who are continuing to receive enzalutamide, having previously responded to enzalutamide during Cycle 0), immunotherapy or investigational medicinal products (IMPs) during the previous 4 weeks before first dose of IMP.
2. Patients with ongoing toxic manifestations of previous treatments greater than NCI CTCAE Grade 1. Exceptions apply.
3. Patients with symptomatic brain or leptomeningeal metastases should be excluded. Exceptions apply.

4. Women of child-bearing potential (or are already pregnant or lactating). Exceptions apply.
5. Male patients with partners of child-bearing potential. Exceptions apply.
6. Major surgery from which the patient has not yet recovered.
7. At high medical risk because of non-malignant systemic disease including active uncontrolled infection.
8. Known to be serologically positive for hepatitis B, hepatitis C or human immunodeficiency virus infection. Patients with previous hepatitis C exposure but no current infection are eligible to participate.
9. Known or suspected hypersensitivity reaction to previous biological therapy that in the opinion of the Investigator is a contraindication for their participation in this study.
10. Concurrent congestive heart failure, prior history of ≥ Class II cardiac disease (New York Heart Association), clinically significant cardiac ischaemia or clinically significant cardiac arrhythmia. Patients with significant cardiovascular disease as defined in the protocol are excluded.
11. Active autoimmune disease. Exceptions apply.
12. Patients receiving doses of prednisolone 10 mg daily (or equipotent doses of other corticosteroids) within 7 days prior to the first dose of study drug are not eligible unless administered as pre-medication.
13. Patients having received a live vaccination within 4 weeks prior to first dose of HMBD-001.
14. Is a patient or plans to participate in another interventional clinical trial, whilst taking part in this Phase 1/2a trial of HMBD-001. Participation in an observational trial or interventional clinical trial which does not involve administration of an IMP and which would not place an unacceptable burden on the patient in the opinion of the Investigator and Medical Advisor would be acceptable.
15. Any other condition which in the Investigator’s opinion would not make the patient a good candidate for the clinical trial.
16. Current or prior malignancy which could affect safety or efficacy assessment of the IMP or compliance with the protocol or interpretation of results. Patientts with curatively-treated non-melanoma skin cancer, non-muscle-invasive bladder cancer, or carcinomas-in-situ are generally eligible.

Part B Arm 1: HMBD-001 and Enzalutamide Combination.
17. Patients receiving warfarin or coumarin-like anti-coagulants.
18. History of seizures or other risk factors for the development of seizures e.g. prior history of stroke, brain injury, brain metastases, leptomeningeal disease.
19. Patients with hypersensitivity to enzalutamide or any of the excipients.
20. Patients who have received prior enzalutamide or other next generation hormonal agent that has been stopped due to toxicities or intolerance or required a dose reduction during administration due to toxicity or intolerance.

Date of first enrolment
07/10/2021

Date of final enrolment
19/08/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Marsden NHS Foundation Trust
-
London
England
SM2 5PT

Study participating centre
Churchill Hospital
-
Oxford
England
OX3 7LE

Study participating centre
Freeman Hospital
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Newcastle
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NE7 7DN

Study participating centre
The Christie NHS Foundation Trust
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Manchester
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M20 4BX

Sponsor information

Organisation
Cancer Research UK

ROR
https://ror.org/054225q67

Funder(s)

Funder type
Not defined

Funder Name
Cancer Research UK

Results and Publications

Individual participant data (IPD) sharing plan
Data from this trial and the final clinical study protocol will be submitted to a public registry and will be available immediately following publication, with no end date. Individual deidentified patient data that underlie the results reported will be shared with researchers whose proposed use of the data is approved by a review committee of the Sponsor. All requests made within 5 years from the end of trial will be considered; requests made subsequently will be considered where possible. Requests should be submitted to drugdev@cancer.org.uk.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results		01/10/2023	30/09/2026	No	No
Abstract results		01/10/2023	30/09/2026	No	No
Basic results		12/08/2026	01/09/2026	No	No
Plain English results		09/09/2026	23/09/2026	No	Yes
Protocol file	version 7.0	04/08/2026	01/09/2026	No	No