

# A Phase I/II trial of UCB4594 in participants with advanced cancer

<b>Submission date</b> 17/10/2023	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 24/01/2024	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 12/05/2026	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

This clinical trial is looking at UCB4594. This is the first time the drug is being tested in humans. UCB4594 is a type of drug called a monoclonal antibody. It has been designed to work by targeting a protein called HLA-G that is found in high levels on some cancer cells. By attaching itself to this protein it may help the immune system to attack and kill the cancer cells.

The four main aims of the clinical trial are to find out:

1. The best dose of UCB4594 that can be given safely to participants in the trial.
2. What the side effects of UCB4594 are and how they can be managed.
3. What happens to UCB4594 inside the body and how it affects cancer cells.
4. Whether UCB4594 can cause cancer to shrink.

### Who can participate?

Patients aged 18 years and over with advanced solid tumours that do not respond to conventional treatment, or for which no conventional therapy is considered appropriate by the Investigator or is declined by the participant

### What does the study involve?

This clinical trial is split into two phases.

Phase I is the 'dose escalation' phase. This is where small groups of participants receive UCB4594 at a certain dose level starting with a low dose level. After reviewing the results obtained at each dose level, it will be decided whether or how much to increase the dose for the next group of participants. This part of the study aims to find the best dose to give that does not cause too many side effects.

Phase II is the 'dose expansion' phase. This starts when the dose escalation phase has worked out the best dose of UCB4594 to give. In this part of the trial UCB4594 will be given alone or in combination with other anti-cancer drugs. This will allow us to find out more about how the drug is working and whether UCB4594 affects cancer.

### What are the possible benefits and risks of participating?

UCB4594 is a new drug that has never been given to humans before. Possible risks and benefits

are based on laboratory tests and experience with similar drugs but there is not yet any information about the effects of UCB4594 in humans. Participants in the trial will be monitored closely to find out the effects of UCB4594.

Where is the study run from?  
Cancer Research UK

When is the study starting and how long is it expected to run for?  
October 2023 to November 2029

Who is funding the study?  
Cancer Research UK

Who is the main contact?  
Prof. Fiona Thistlethwaite, [the-christie.ecmt.enquiries@nhs.net](mailto:the-christie.ecmt.enquiries@nhs.net)

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-a-drug-called-ucb4594-for-cancer-that-has-spread>

## Contact information

### Type(s)

Scientific, Principal investigator

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**Additional identifiers****ClinicalTrials.gov (NCT)**

NCT06380816

**Integrated Research Application System (IRAS)**

1008098

**Central Portfolio Management System (CPMS)**

58100

**Protocol serial number**

CRUKD/24/001

**Study information****Scientific Title**

A Cancer Research UK Phase I/II trial to assess the safety, tolerability, pharmacokinetics and preliminary anti-tumour activity of UCB4594 alone and in combination with anti-cancer treatments in participants with advanced malignancies

**Study objectives**

Primary objectives:

1. To find out the best dose or doses of UCB4594 that can be given safely to participants on its own and with other anti-cancer drugs
2. To assess how safe and tolerated the best dose or doses of UCB4594 identified are when UCB4594 is given to participants on its own or with other anti-cancer drugs for up to one year.

Secondary objectives:

1. To determine if there is any anti-cancer activity of UCB4594 in participants with advanced solid tumours, both on its own and with other anti-cancer drugs
2. To monitor levels of UCB4594 in the blood
3. To further assess the safety and tolerability profile of UCB4594 both on its own and in combination with other anti-cancer drugs

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Approved 12/12/2023, North East – York Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)207 104 8079; york.rec@hra.nhs.uk), ref: 23/NE/0170

## **Study design**

Multi-centre first-in-human non-randomized Phase I/II dose escalation and dose expansion trial

## **Primary study design**

Interventional

## **Study type(s)**

Efficacy, Safety

## **Health condition(s) or problem(s) studied**

Advanced solid tumours

## **Interventions**

Dose escalation phase: Participants will receive UCB4594 as an intravenous infusion once every 3 weeks. The dose administered will be between 3 mg and 1600 mg.

Expansion phase: Participants will receive UCB4594 as an intravenous infusion once every 3 weeks. The dose of UCB4594 as monotherapy and in combination with other anti-cancer treatments and the dose of the combination agents will be determined based on data from the dose escalation phase and the choice of combination agent.

All participants may receive UCB4594 for up to 18 cycles (~1 year) and will be followed up for up to 6 months after their last dose.

## **Intervention Type**

Drug

## **Phase**

Phase I/II

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

UCB4594

## **Primary outcome(s)**

1. The recommended Phase 2 dose (RP2D) of UCB4594 will be determined both for UCB4594 on its own and with other anti-cancer drugs, based on the maximum tolerated dose or maximum administered dose (MTD/MAD) and all available safety, efficacy, pharmacokinetic (PK) and pharmacodynamic data (all modules – dose escalation [module A], monotherapy dose expansion [module B] and any combination modules [module C]). Evaluation of this endpoint will occur once all patients in each module (Module A, B or C) have completed the dose-limiting toxicity (DLT) assessment period (21 days) and all relevant data has been collected.

2. The frequency of adverse events (AEs) considered at least possibly related to UCB4594. AE data will be collected for UCB4594 (all modules) and in combination with other anti-cancer treatments (Module C), and the number of Grade 3, 4 and 5 AEs at least possibly related to UCB4594 (all modules) and with other anti-cancer treatments (Module C) for up to 18 cycles (~12 months) of dosing determined. AEs, including relatedness, seriousness and severity according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE)

Version 5.0, will be assessed by the Investigator. Evaluation of this endpoint will occur once the last patient recruited overall has received up to 18 cycles (~12 months) of UCB4594.

### **Key secondary outcome(s)**

Current key secondary outcomes:

1. Tumour response according to Response Evaluation Criteria in Solid Tumours (RECIST) v1.1 and immune RECIST (iRECIST) (all modules) and Overall Response Rate (ORR) (expansion phase; Modules B and C). ORR is defined as the proportion of participants who achieve complete response (CR/iCR) or partial response (PR/iPR) as the best overall response according to RECIST v1.1 and iRECIST. Response will be assessed at baseline, once every 6–9 weeks, and at End of Treatment.
2. The PK parameters of UCB4594 (including maximum concentration, minimum concentration, area under the curve, steady state volume of distribution, clearance, and terminal elimination half-life) (monotherapy modules; Modules A and B). UCB4594 concentrations will be measured in serum in samples collected from participants at up to 18 timepoints during Cycles 1 to 2, two timepoints for every subsequent cycle, and at the End of Treatment Visit for Module A (dose escalation); 2 samples will be taken for every cycle, and a further sample at the End of Treatment Visit for Module B (monotherapy expansion).
3. The frequency of AEs considered at least possibly related to UCB4594. The frequency of AEs will be assessed for UCB4594 (all modules) and/or with other anti-cancer treatments (Module C), and the number of Grade 3, 4 and 5 AEs at least possibly related to UCB4594 (all modules) and/or other anti-cancer treatments (Module C) determined. AEs, including relatedness, seriousness and severity according to NCI CTCAE Version 5.0, will be assessed by the Investigator. AEs are collected from the date of informed consent until 6 months after the last dose of UCB4594.

Previous key secondary outcomes:

1. Tumour response according to Response Evaluation Criteria in Solid Tumours (RECIST) v1.1 and immune RECIST (iRECIST) (all modules) and Overall Response Rate (ORR) (expansion phase; Modules B and C). ORR is defined as the proportion of participants who achieve complete response (CR/iCR) or partial response (PR/iPR) as the best overall response according to RECIST v1.1 and iRECIST. Response will be assessed at baseline, once every 6–9 weeks, and at End of Treatment.
2. The PK parameters of UCB4594 (including maximum concentration, minimum concentration, area under the curve, steady state volume of distribution, and clearance) (monotherapy modules; Modules A and B). UCB4594 concentrations will be measured in serum in samples collected from participants at up to 18 timepoints during Cycles 1 to 2, two timepoints for every subsequent cycle, and at the End of Treatment Visit for Module A (dose escalation); 2 samples will be taken for every cycle, and a further sample at the End of Treatment Visit for Module B (monotherapy expansion).
3. The frequency of AEs considered at least possibly related to UCB4594. The frequency of AEs will be assessed for UCB4594 (all modules) and/or with other anti-cancer treatments (Module C), and the number of Grade 3, 4 and 5 AEs at least possibly related to UCB4594 (all modules) and/or other anti-cancer treatments (Module C) determined. AEs, including relatedness, seriousness and severity according to NCI CTCAE Version 5.0, will be assessed by the Investigator. AEs are collected from the date of informed consent until 6 months after the last dose of UCB4594.

**Completion date**

01/11/2029

## **Eligibility**

## **Key inclusion criteria**

1. Written (signed and dated) informed consent and capable of co-operating with IMP administration and follow-up.
2. Participant population: Histologically or cytologically proven advanced solid tumours (as specified below), refractory to conventional treatment, or for which no conventional therapy is considered appropriate by the Investigator or is declined by the participant. Module A (dose escalation): Tumour types which have shown high levels of human leucocyte antigen (HLA)-G expression (as reported in the literature): head and neck squamous cell carcinoma, non-small cell lung cancer, colorectal cancer, triple-negative breast cancer, renal cell cancer (clear cell only), oesophago-gastric cancer (excluding gastrointestinal stromal tumour), cervical cancer, ovarian cancer, pancreatic cancer. N.B. Participants with small cell type cancers on histology/cytology are excluded. Pre-treatment biopsies are mandatory for all participants. Paired biopsies will be mandatory for participants from doses of 30 mg and higher. Participants must have disease amenable to biopsy (excluding bone metastases) as deemed safe by the Investigator.
3. Measurable disease, according to RECIST v1.1
4. Life expectancy of at least 12 weeks
5. Eastern Cooperative Oncology Group performance status of 0 or 1
6. Haematological and biochemical indices within defined ranges. These measurements should be performed to confirm the patient's eligibility to participate in the trial.
7. Aged 18 years or over at the time consent is given. Participants aged 16–17 years may be eligible for recruitment to the backfill cohorts in dose escalation once adequate safety and toxicity data have been established in participants aged 18 years or over. All relevant data will be reviewed and a decision on the inclusion of participants aged 16–17 years will be made by the Trial Management Group.

## **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**

1. Radiotherapy (except palliative), endocrine therapy (unless for non-malignant disease), chemotherapy, targeted therapy or immunotherapy, or any other investigational medicinal products (IMPs) during the previous 4 weeks or 5 half-lives (whichever is shorter) before the first dose of IMP

2. Ongoing toxicity of previous treatments >CTCAE Grade 1 (except alopecia of any grade, stable Grade 2 peripheral neuropathy or hormone-replacement therapy (HRT)-managed endocrine disorders)
3. Patients with rapidly progressing / symptomatically deteriorating brain/leptomeningeal metastases/untreated brain metastases are excluded. Patients with previously treated brain metastases are eligible if they haven't had a seizure or a clinically significant change in neurological status or required steroids in the last 2 weeks
4. Pregnant or breastfeeding female patients (or planning to breastfeed)
5. Women of childbearing potential. However, those not already pregnant or breastfeeding (or discontinue breastfeeding) and meet the following are eligible:
  - 5.1. Have a negative serum pregnancy test within 7 days before enrolment and either:
    - 5.2.1. Agree to a form of highly effective contraception plus a barrier method, or
    - 5.2.2. Agree to sexual abstinenceEffective from the negative pregnancy test, throughout the trial and for 10 months after the last dose of UCB4594.
6. Male patients with partners of childbearing potential. However, patients who meet the following are eligible:
  - 6.1. Agree to a barrier method of contraception or sexual abstinence
  - 6.2. Males with pregnant or breastfeeding partners must use barrier method contraception to prevent exposure of the foetus or neonate
  - 6.3. Non-vasectomised males must also ensure any partner of childbearing potential uses highly effective contraception or agrees to sexual abstinenceEffective from the date of the first dose of UCB4594, throughout the trial and for 5 months after the last dose of UCB4594
- N.B. Males must refrain from donating sperm for the same period
7. Surgery from which the patient has not yet recovered
8. High medical risk because of non-malignant systemic disease, including serious or uncontrolled infection (requiring IV antibiotics) or unexplained fever >38°C within 2 weeks prior to the first dose of UCB4594
9. Known to be serologically positive for hepatitis B virus, hepatitis C virus or human immunodeficiency virus
10. Active or suspected autoimmune disease, or any history of autoimmune condition that required systemic corticosteroids or immunosuppressive agents. Patients who have ever had a transplant are excluded. This does not apply to patients with: vitiligo, alopecia, or type I diabetes mellitus, psoriasis not requiring chronic systemic immunosuppressive treatment within the past 2 years, stable autoimmune-mediated hypothyroidism on HRT, and Raynaud's syndrome
11. Are being treated with escalating or supraphysiologic doses of corticosteroids or immunosuppressive agents. Participants with immunotherapy-related hypophysitis adequately treated with physiologic doses of steroids are not excluded. Use of topical, ophthalmic, inhaled, intermittent steroid injections, and intranasal corticosteroids are permitted
12. Hypersensitivity to the ingredients/excipients (including polysorbate 80) in UCB4594
13. History of significant toxicities from treatment of immune checkpoint inhibitors (CPIs) that necessitated permanent discontinuation (Patients who started on combination CPI [e.g., ipilimumab/nivolumab] and had toxicity requiring discontinuation of one CPI [e.g., continued with nivolumab single agent] are not excluded)
14. History of Grade  $\geq 3$  infusion-related reaction to monoclonal antibodies or similar drugs
15. Prior treatment with HLA-G, immunoglobulin-like transcript (ILT)2 or ILT4-targeting drug
16. Live, attenuated vaccine within 28 days prior to the first dose of IMP
17. Increased risk due to tumour flare (e.g., an initial increase in tumour size that may lead to obstruction of airways, etc)
18. Significant active pulmonary disease or condition at screening, including:
  - 18.1. Lymphangitis carcinomatosa

- 18.2. History of interstitial lung disease or pulmonary fibrosis
- 18.3. History of pulmonary inflammatory disease
19. Evidence of bleeding diathesis
20. Significant cardiovascular disease, defined as a history of: congestive heart failure requiring therapy or left ventricular ejection fraction <40%, unstable angina pectoris or myocardial infarction within 6 months prior to entry, or current poorly controlled angina (symptoms weekly or more), clinically significant cardiac arrhythmia within 6 months prior to entry (asymptomatic atrial fibrillation or asymptomatic first-degree heart block permitted), or myocarditis. Presence of symptomatic or severe valvular heart disease. Baseline QT interval corrected by Fridericia >450 msec for males and >470 msec for females on triplicate electrocardiogram is ineligible
21. Participant in or plans to join another interventional trial
22. Other current malignancies. Cancer survivors who have undergone potentially curative therapy for prior malignancy with no evidence of disease for 3+ years are eligible
23. Any other condition that, in the Investigator's opinion, means the trial is not in the patient's best interest

**Date of first enrolment**

25/06/2024

**Date of final enrolment**

01/11/2028

## **Locations**

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**The Christie NHS Foundation Trust**

550 Wilmslow Road

Withington

Manchester

England

M20 4BX

**Study participating centre**

**University Hospital Southampton NHS Foundation Trust**

Southampton General Hospital

Tremona Road

Southampton

England

SO16 6YD

**Study participating centre**  
**Freeman Hospital**  
Freeman Road  
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Newcastle upon Tyne  
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NE7 7DN

**Study participating centre**  
**Guys Hospital**  
Great Maze Pond  
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SE1 9RT

## Sponsor information

**Organisation**  
Cancer Research UK

**ROR**  
<https://ror.org/054225q67>

## Funder(s)

**Funder type**  
Charity

**Funder Name**  
Cancer Research UK

**Alternative Name(s)**  
CR\_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

**Funding Body Type**  
Private sector organisation

**Funding Body Subtype**  
Other non-profit organizations

**Location**  
United Kingdom

# 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 participant 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](mailto:drugdev@cancer.org.uk).

## IPD sharing plan summary

Available on request