

# Enabling genomic testing in cancer of unknown primary

<b>Submission date</b>	<b>Recruitment status</b>	<input checked="" type="checkbox"/> Prospectively registered
07/06/2024	Recruiting	<input checked="" type="checkbox"/> Protocol
<b>Registration date</b>	<b>Overall study status</b>	<input type="checkbox"/> Statistical analysis plan
15/08/2024	Ongoing	<input type="checkbox"/> Results
<b>Last Edited</b>	<b>Condition category</b>	<input type="checkbox"/> Individual participant data
09/01/2025	Cancer	<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Cancer of Unknown Primary (CUP) is where cancer cells are found in the body but the place the cancer began is not known. It is the 6th leading cause of cancer death in the UK and the prognosis is poor with a median survival of 6-9 months. There is a higher than average incidence of CUP in the North West (NW) of England (population of 7.4 million). Precision medicine has transformed treatment strategies in known tumour types, however in CUP there remains an urgent need to better understand CUP molecular characteristics to establish potential roles for novel therapeutic strategies. Treatment options remain limited due to difficulties in determining the primary site of the tumour and the lack of access to validated biomarkers. Access to good-quality tissue for molecular profiling remains a huge challenge in CUP. The emergence of liquid biopsies (sequence DNA in a blood test) as a source of biomarkers is also gaining rapid ground and this study aims to explore the potential utility of liquid biopsies in CUP.

### Who can participate?

Patients aged 16 years or over with Cancers of Unknown Primary

### What does the study involve?

Participants will attend a baseline visit where their medical history and some clinical data will be collected and recorded by the study team. Adverse and serious adverse event information will be collected throughout. Additional clinical data will be recorded once participants have progressed on their treatment and to follow participants up, up to 12 months later.

At baseline, the following samples will be collected:

1. Up to 40 ml of blood
2. Archival tumour blocks from a previous biopsy will be retrieved/requested. Samples will only be sent for analysis if blood samples fail to report a result.

When participants progress from their treatment, the following samples will be collected:

1. Up to 20 ml of blood

Samples will be sent to collaboration research laboratories for DNA analysis. The results from this analysis will be reported back to the participant's research team.

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

Although the objectives of this study are not directly therapeutic and therefore may not have a

direct benefit for all participants, it is anticipated that the results from the tests may help direct some participants to a suitable treatment option. There is also the benefit of increased knowledge about molecular changes in their cancer which some patients may also find useful. General risks associated with data collection apply. Minor risks are associated with blood sample collection such as bruising and pain. Genetic research may result in psychological distress if results show other previously unknown conditions (e.g., hereditary conditions). All participants will receive the appropriate information about this at the time of consent and will be given the option to not have any such results disclosed.

Where is the study run from?  
The Christie (lead centre) (UK)

When is the study starting and how long is it expected to run for?  
December 2023 to February 2028

Who is funding the study?  
NIHR Academy (UK)

Who is the main contact?  
Dr Natalie Cook, the-christie.egg-cup@nhs.net

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-to-learn-more-about-the-causes-of-cancer-of-unknown-primary-egg-cup>

## Contact information

### Type(s)

**Contact name**  
Dr Matthew Concannon

**Contact details**  
The Christie NHS Foundation Trust  
Wilmslow Road  
Manchester  
United Kingdom  
M20 4BX  
+44 (0)161 918 7276  
the-christie.egg-cup@nhs.net

**Type(s)**  
Principal investigator

**Contact name**  
Dr Natalie Cook

**Contact details**  
The Christie NHS Foundation Trust  
Wilmslow Road  
Manchester  
United Kingdom

M20 4BX  
+44 (0)161 918 7276  
the-christie.egg-cup@nhs.net

## Additional identifiers

### Clinical Trials Information System (CTIS)

Nil known

### Integrated Research Application System (IRAS)

332987

### ClinicalTrials.gov (NCT)

Nil known

### Protocol serial number

CPMS 62840, IRAS 332987, NIHR303220

## Study information

### Scientific Title

Enabling Genomic Testing in Cancer of Unknown Primary (EGG-CUP)

### Acronym

EGG-CUP

### Study objectives

Does integrating circulating free DNA testing into routine care assist with the diagnosis and/or stratification of patients diagnosed with Cancer of Unknown Primary (CUP)?

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

Approved 28/06/2024, North West - Haydock Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)207 104 8032; haydock.rec@hra.nhs.uk), ref: 24/NW/0181

### Study design

Both; Design type: Diagnosis, Other, Clinical Laboratory Study

### Primary study design

Interventional

### Study type(s)

Treatment

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

Cancer of unknown primary

### Interventions

**Study population:**

Patients with a confirmed diagnosis of Cancer of Unknown Primary (CUP) will be recruited from six North-West-based NHS hospitals.

**Consent:**

All participants will be provided with a patient information sheet (PIS) and will be given sufficient opportunity to review and ask questions about the information before being asked to voluntarily consent to the study. Consent will be obtained by an appropriately trained and delegated member of the study team at a point that they are confident the participant fully understands the information they have received.

**Data collection:**

Only once fully informed consent has been obtained, participants will attend a baseline visit. During this visit their medical history and some clinical data will be collected and recorded by the study team. Adverse and serious adverse event information will be collected throughout. Additional clinical data will be recorded once participants have progressed on their treatment and to follow participants up, up to 12 months post baseline.

**Sample collection:**

At baseline, the following samples will be collected:

1. Up to 40 ml blood for circulating tumour DNA (ctDNA) and STRECK samples.
2. Archival tumour blocks from a prior biopsy will be retrieved/requested. Samples will only be sent for analysis if blood samples fail to report a result.

When participants progress from their treatment, the following samples will be collected:

1. Up to 20 ml blood for circulating tumour DNA (ctDNA)

Samples will be sent to collaboration research laboratories at Penzburg, Germany (or Boston, USA as a backup) for circulating tumour DNA (ctDNA) analysis. The results from this analysis will be reported back to the participant's research team and will be discussed in the molecular tumour board.

STRECK blood samples will be processed and transferred to the Cancer Biomarker Centre to be used for research of a methylation assay.

**Intervention Type**

Other

**Phase**

Not Specified

**Primary outcome(s)**

The utility of cfDNA molecular profiling in patients diagnosed with CUP as determined by:

1. Percentage of patients with adequate cfDNA yields measured using FoundationOne® Liquid CDx testing of blood samples obtained at baseline or progression timepoints
2. Percentage of patients with actionable genomic alterations measured using FoundationOne® Liquid CDx testing of blood samples obtained at baseline or progression timepoints
3. Percentage of patients eligible for personalised treatment options or enrolment on a UK-based clinical trial because of the cfDNA results, measured using FoundationOne® Liquid CDx testing of blood samples obtained at baseline or progression timepoints

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

1. Documentation and feedback of genomic results/GTAB outcomes to all patients and treating teams following FoundationOne® CDx or FoundationOne® Liquid CDx at baseline, and FoundationOne® Liquid CDx at progression
2. Routinely incorporate molecular genomics as standard of care in patients diagnosed with CUP (working with the NHS England Genomic Medicine Service) following FoundationOne® CDx or FoundationOne® Liquid CDx at baseline and FoundationOne® Liquid CDx at progression
3. Develop a data collection repository and readily available information on trials/treatments for patients diagnosed with CUP to be shared at monthly trial management group meetings to ensure that investigators are aware of suitable trial opportunities

## **Completion date**

11/02/2028

## **Eligibility**

### **Key inclusion criteria**

1. Aged 16 years or over
2. Written informed consent according to Good Clinical Practice (GCP) and national regulations
3. Eastern Cooperative Oncology Group (ECOG) Performance status 0-2
4. Confirmed diagnosis of CUP as per the European Society for Medical Oncology (ESMO) guidelines. Patients must have:
  - 4.1. The local pathology reports confirming compatibility with CUP diagnosis and the associated slides used for the diagnosis
  - 4.2. Discussion at a local CUP MDT confirming diagnosis
5. Availability of archival tumour histological report.
6. Willingness to provide blood samples on up to two occasions during the study

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

16 years

### **Sex**

All

### **Key exclusion criteria**

1. Patient with an immunohistochemistry profile that provides a definitive clinical indication of a primary cancer with a specific treatment
2. Known HIV, Hepatitis B, C positive, due to the difficulties in handling high-risk specimens
3. Patients who are unable to provide fully informed written consent
4. Presence of any medical, psychological, familial or sociological condition that, in the investigator's opinion, will hamper compliance with the study protocol and follow-up schedule

5. Bleeding diathesis (patients on anticoagulation are permitted to enter the trial if anticoagulation can be safely managed to enable blood sampling)
6. Conditions in which blood sampling may increase the risk of complications for the patients and /or investigator

**Date of first enrolment**

15/08/2024

**Date of final enrolment**

01/12/2026

## Locations

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**The Christie**  
550 Wilmslow Road  
Withington  
Manchester  
United Kingdom  
M20 4BX

**Study participating centre**

**Clatterbridge Cancer Centre**  
65 Pembroke PLACE  
Liverpool  
United Kingdom  
L7 8YA

**Study participating centre**

**Northern Care Alliance**  
Mayo Building  
Salford Royal  
Stott Lane  
Salford  
United Kingdom  
M6 8HD

**Study participating centre**

**Lancashire Teaching Hospitals NHS Foundation Trust**

Royal Preston Hospital  
Sharoe Green Lane  
Fulwood  
Preston  
United Kingdom  
PR2 9HT

**Study participating centre****University Hospitals of Morecambe Bay NHS Foundation Trust**

Westmorland General Hospital  
Burton Road  
Kendal  
United Kingdom  
LA9 7RG

**Study participating centre****Blackpool Teaching Hospitals NHS Foundation Trust**

Victoria Hospital  
Whinney Heys Road  
Blackpool  
United Kingdom  
FY3 8NR

## **Sponsor information**

**Organisation**

The Christie NHS Foundation Trust

**ROR**

<https://ror.org/03v9efr22>

## **Funder(s)**

**Funder type**

Government

**Funder Name**

NIHR Academy

# Results and Publications

## Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be published as a supplement to the results publication

## IPD sharing plan summary

Published as a supplement to the results publication

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Participant information sheet</a>	version 1.1	24/06/2024	13/08/2024	No	Yes
<a href="#">Participant information sheet</a>	version 1.2	07/08/2024	15/08/2024	No	Yes
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Protocol file</a>	version 1.1	25/06/2024	13/08/2024	No	No