ISRCTN42910771 https://doi.org/10.1186/ISRCTN42910771

Enabling genomic testing in cancer of unknown primary

Submission date 07/06/2024	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 15/08/2024	**Overall study status** Ongoing	
Last Edited 09/01/2025	**Condition category** Cancer	

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

Integrated Research Application System (IRAS)
332987

Central Portfolio Management System (CPMS)
62840

National Institute for Health and Care Research (NIHR)
303220

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

Primary study design
Interventional

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

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 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?
Participant information sheet	version 1.1	24/06/2024	13/08/2024	No	Yes
Participant information sheet	version 1.2	07/08/2024	15/08/2024	No	Yes
Protocol file	version 1.1	25/06/2024	13/08/2024	No	No