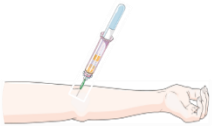
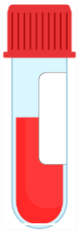
EGG-CUP Summary Sheet

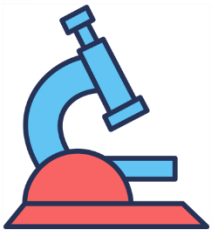
THIS SUMMARY SHEET PROVIDES A BRIEF OVERVIEW OF THE STUDY AND IS NOT A SUBSTITUTE OR REPLACEMENT FOR THE PATIENT INFORMATION SHEET

STUDY PURPOSE

- This study aims to better understand the genetics of Cancer of Unknown Primary (CUP).
- Genetic testing looks for changes in your DNA (known as mutations) which may be significant for your cancer.
- This type of testing can sometimes help doctors select treatments for patients that target these changes.
- There is a genetic test that can be done using a blood sample.
- Patients diagnosed with CUP are not currently always able to access this blood test


We will take a blood sample and send it for testing. We would also like to use a sample together with the data collected about you during the study to help us to predict the location of the primary cancer. In some cases, we will require a tumour tissue sample be sent for testing.




Your results will go to your doctor and be discussed at a meeting.

The doctor will inform you of the results.
If there are no significant results your current and future treatments will not be affected.

We will follow you for up to 1 year from the date of consent.

We will ask if you would like to donate your previous tumour tissue sample for future research

EGG-CUP

Enabling Genomic Testing in Cancer of Unknown Primary

We invite you to take part in this research study because you are a patient with a cancer of unknown primary (CUP).

Joining the study is entirely up to you. Before you decide whether to take part, we would like you to understand why the research is being done and what it will involve for you.

Please take time to read the following information carefully. Discuss it with friends and relatives if you wish.

Ask us if there is anything that is not clear or if you would like more information.

Important things that you need to know

In the case of CUP, it is particularly important to get as much diagnostic information as possible to help identify the best possible treatment. The purpose of this study is to better understand the changes that have happened within your cells which have resulted in your diagnosis of cancer (the genetic characteristics of your cancer). We hope to be able to use this information to guide treatment choices and to produce a tool that may help us understand what your response to treatment(s) may be.

If you choose to take part, you can stop taking part in the study at any time.

If you choose not to take part this will not impact the standard of care or other treatments, you are receiving now or in the future.

In this research study we will use information from you/your medical records/your GP. We will only use information that we need for the research study. We will protect your confidentiality and only share your personal details on a need to know basis for the study.

Everyone involved in this study will keep your data safe and secure. We will also follow all privacy rules.

At the end of the study we will save some of the data in case we need to check it/for future research.

We will make sure no-one can work out who you are from the reports we write. The full information sheet will tell you more about this.

Contents

How to contact us

If you have any questions about this study, please talk to the doctors who organise it: Dr Natalie Cook on 0161 918 7672 (Secretary) or Project Manager 0161 918 7672.

1 Why are we doing this study?

The purpose of this study is to understand the changes that have happened within your cells which have resulted in your diagnosis of cancer (the genetic characteristics of your cancer). To date, there have only been limited clinical and scientific studies for CUP to look at new ways of testing for changes that have happened within your cells to cause your cancer and where in the body those changes have happened; and to compare these to the current standard tests to support your clinical team in making the best decisions on your treatment.

To analyse the genetic characteristics of your cancer a blood sample will be tested, where the test fails to identify any changes (mutations) we will require a tumour tissue sample be sent for testing if applicable. This will help us to determine if a blood sample is a suitable test for patients diagnosed with CUP and also help inform the most appropriate diagnostic choices for CUP in the future.

Your genetic results from this study will be provided to you and your hospital CUP team and may be used to inform your suitability to receive an experimental treatment in the future. If an appropriate experimental treatment is available for you, you will be given further details and asked to sign a separate consent form to receive that treatment.

This study is open to patients diagnosed with CUP, who are fit enough for treatment of their cancer. The study will be open to recruitment from mid 2024 until either 100 participants have been recruited or December 2026, whichever comes first.

2 Why have I been invited to take part?

You have been invited to take part because you have a diagnosis of Cancer of Unknown Primary (CUP) and understanding the genetic characteristics of this cancer may help to determine future treatment options and possibly give us more information about where in your body the primary cancer might have originated.

3 What will happen if I take part?

Taking part in this study is completely voluntary. We will describe the study and go through this information sheet during a consultation, a member of the study team will determine if you are eligible to take part. You will be given a copy of the information sheet to take home, you will have ample time to read the information and discuss it with your family or friends if you wish. If you are agreeable, we will then ask you to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

We will ask your permission to provide the following samples, and agreements which are required for the study:

a) Blood samples (up to 40 mls, roughly 3 tablespoons) at the beginning of the study, and dependent upon treatment outcome during the follow up period a further 17mL (roughly 1 tablespoon). Every effort will be made to take the blood samples at the same time as your routine blood tests at clinic visits. The extra blood samples will not increase the amount of time you spend in hospital.

b) The donation of a sample of your archival tumour tissue, taken from a previous biopsy or operation.

c) Your GP will be informed of your participation in the study and of any relevant results.

d) Your consent for information to be collected about you such as your date of birth, diagnosis and previous treatments. We will also collect some information to follow up on your treatment journey for up to 12 months

after you enroll onto the study. This information will be obtained by telephone contact with you or your GP or from your health records.

e) Your consent to your anonymised genetic data being shared on a public database. Data generated from this study could be used to explore a wide range of additional research questions, and data from multiple different projects can be combined to help speed up discoveries that improve the ability to diagnose, treat, and prevent cancer.

f) You will be asked to consent to storage of tissue and blood samples for research now and in the future for studies aiming to improve knowledge and treatment of cancers.

This data, alongside clinical data collected about you (listed on page number 6) will be stored on a secure server at The Christie NHS Foundation Trust for up to 5 years. The study collaborators will have access to this data. All data stored on this server will be pseudo-anonymised so collaborators will not be able to link the information back to you. Access to your data is restricted as explained in section 7 of this information sheet.

What tests will be performed on my samples and where will this happen?

We will analyse genetic material (DNA/RNA) from your samples.

Your blood and/or tissue samples will be analysed by Foundation Medicine Inc who have laboratories in Boston, USA and Penzberg, Germany. Foundation Medicine's analysis generates additional genetic information when producing a report on the sample. This additional information will be returned to The Christie NHS Foundation Trust with the report. The Christie NHS Foundation Trust may only use the additional information in this study or future research carried out by The Christie NHS Foundation Trust. Blood samples sent off for analysis will all be used up, or any that may be leftover will be destroyed. Foundation Medicine will retain used tissue slides for up to 10 years with any unused tissue samples returned to the participating hospital.

Blood samples will also be sent to the Cancer Research UK Cancer Biomarker Centre, UK, for further research analysis. Blood samples sent off for analysis will all be used up, or any that may be leftover will be destroyed.

If you give your consent, any unused samples at the end of this study will be gifted for use in future research projects. Your samples may be donated to a biobank who will make your samples available to all kinds of researchers, including pharmaceutical companies for all kinds of cancer research, including genetic studies. Access to your samples will be strictly regulated and used with all of required ethics permissions in place. Researchers using samples will only ever receive pseudo-anonymised data and your personal identifiable information will kept strictly confidential.

All your samples will be coded using a unique study identifier. Additional information such as your initials may be required by laboratory staff. If this data is sent, it will be handled according to the Data Protection Act and General Data Protection Regulation 2018. Only doctors and key study personnel will have access to any identifiable information.

The collaborators will receive information about you such as: your year of birth and gender; information on your cancer diagnosis and previous treatments you have had; information on tests you have undergone, or undergo whilst on study such as scans and blood test results. Any information received by the collaborators will be pseudo-anonymised, meaning it will be linked to you by a unique trial identifier. Only your local research team will be able to match this identifier back to you personally.

Will the researchers give me results?

The main reason for performing this research is to find genetic changes in your cancer that may help your doctor to understand more about what is causing your cancer and to guide your doctors in possible future treatment options, based on available information and their best clinical judgement.

A scientific panel consisting of experts in cancer, genetics and ethics will serve on a 'Molecular Tumour Board' that will review the results and determine whether the results could help with future treatment plans. We will always tell you about results that have a direct impact on the care of your current cancer.

Our default position will be to give you all of the information that we receive from your test. However, if you would prefer not to receive it, you will need to sign the relevant box on the attached consent form stating that you would not wish to receive this information.

There are two kinds of information that do not have direct impact on your cancer but which you may or may not wish to know about:

i) Results that may have significance for your biological family members. For example, we may discover that you have a gene that, if inherited by your biologically-related family members, could increase their risk of cancer or other medical conditions. Your family members may or may not have inherited that gene – they would have to be tested to find out. It is important to consider whether you and/or your family would want to know about this.

ii) Results that are not related to your cancer, but may have potential medical impact for you. For example, we may discover a gene that increases your risk of another medical condition, not related to your cancer. It is important to consider whether you would want to receive this information.

We will discuss these situations and provide you with genetic counselling if you wish so you are aware of the potential implications of these results. You may also wish to discuss this with your family. We would offer to refer you or your family members to NHS genetic services for further discussion about the implication of the findings should one of these abnormalities be found and you have chosen to receive the results. The genetic specialists may then offer genetic screening to you or your family members.

4 What are the possible benefits of taking part?

With this research we may find genetic changes that have direct impact on the management of your current cancer. If we do not find any information that would be important for your cancer you may not receive any personal benefit from taking part. However, the samples that you donate will be used for research to determine more about the genetics of CUP that may help doctors, scientists and data scientists identify new treatments for patients with CUP in the future.

5 What are the possible disadvantage and risks of taking part?

Blood samples: Blood will be taken by trained nurses and a health care professionals trained to do this procedure. The risks involved in donating blood samples are the same as for routine blood tests. There may be discomfort or pain in the skin and tissue around the vein where the blood is taken. There may be bruising over the vein after the procedure and occasionally people may experience light-headedness or fainting.

Psychological Risks linked to genetic research: Some genetic information may cause you psychological or emotional distress (for instance discovery of previously unknown health problems or findings that you could carry a gene for certain diseases). If you do consent to receive information and if your results show genetic changes

that may affect you or your family in this way, you will have the option to be referred for genetic counselling to discuss the implications of these results.

Data sharing and identification: Your genetic data may be shared on a public database. No personal identifiable data (such as name and address) will be disclosed, however, we may include information on your race, gender, diagnosis and treatments received. Whilst the disclosed information could not identify you it is theoretically possible that the genomic information when combined with information from other public sources could be used to identify an individual, although this is extremely unlikely. The study team will consider carefully which database your genetic data may be shared on.

6 What will happen if I do not want to carry on with the study?

You can withdraw from the study at any time by contacting:

Local contact details

[SITES TO INSERT LOCAL PRINCIPAL INVESTIGATOR, RESEARCH NURSE, STUDY COORDINATOR DETAILS]

<insert relevant contact details/process by which participants can request to be withdrawn from the study>.

If you consent to the study but subsequently become unable to give consent then you will be withdrawn from the study and no further information or samples will be collected. Previously obtained data and samples will still be used in the study.

7 What if I have a concern?

If you have a concern about any aspect of this study, you should speak with any of the research staff or the Chief Investigator, Dr Natalie Cook at the-christie.egg-cup@nhs.net

If you remain unhappy and wish to complain formally, the normal NHS complaints mechanism will be available to you. Details can be obtained from the Patient Advice and Liaison Service at your hospital.

<insert local contact details here>

8 How will we use information about you?

We will need to use information from you/from your medical records/your GP for this research project.

This information will include:

- Your Name and NHS number
- Date or year of birth
- Demographic information (e.g. Ethnicity/Gender/Family History)
- Medical/Oncology History
- Treatment and Outcome information
- Detail of certain tests you have (e.g blood tests, CT scans)

People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure.

Some of your information will be sent to Germany or the United States of America. They must follow our rules about keeping your information safe.

Once we have finished the study, we will keep some of the data so we can check the results, your data will be held for up to 5 years. We will write our reports in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason but we will keep information about you that we already have.

If you choose to stop taking part in the study, we would like to continue collecting information about your health from central NHS records/ your hospital/ your GP. If you do not want this to happen, tell us and we will stop.

We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

You can find out more about how we use your information:

- At www.hra.nhs.uk/information-about-patients
- Our leaflet available from one of your research team
- By asking one of the research team
- By sending an email to the-christie.dpo@nhs.net

9 What will happen to the results of the study?

At the end of the study, the results will be analysed and published in medical journal and/or presented at scientific meetings.

All data will be anonymised and no personal details such as name or address will ever be included in any publications or presentations.

If you would like to obtain a copy of the published scientific results, please ask your doctor.

10 What support can I get whilst being part of the study?

For further information about CUP: please visit CUP Foundation – Jo's friends www.cupfoundjo.org

General information about research – please visit the NHS website: http://www.nhs.uk/Conditions/Clinical-trials/Pages/Introduction.aspx or Cancer Research UK website: http://www.cancerresearchuk.org/about-cancer/trials/types-of-trials/what-clinical-trials-are

General information about genetic testing can be found at
http://www.nhs.uk/Conditions/Genetics/Pages/genetic-testing-and-counselling.aspx (although this website does not specifically provide information about testing genetics of cancer).

Will I be paid?

We are unable to pay you for participating in this study. It is anticipated that samples will be collected at the same time as your usual hospital visits wherever possible. We are unable to pay expenses for any additional visits that may be required.

Further information about cancer, including how to find support:

Cancer Research UK www.cancerresearchuk.org

Macmillian Cancer Support
www.macmillian.org.uk

11 Additional information

Who has organised this study?

The Christie NHS Foundation Trust is legally responsible for the study. The NHS indemnity scheme will apply for any harm arising from the management or conduct of this research. The University of Manchester indemnity will apply for any harm arising from the design of this research.

Who is funding the study?

The National Institute of Health Research (NIHR) in association with the Rosetrees Trust (NIHR award, 30322) is funding this study. Additional service support and testing has been funded by F.Hoffmann-La Roche AG.

Who has reviewed this study?

All research in the NHS is reviewed and approved by an independent group of people, called a Research Ethics Committee. It has also been reviewed by Research and Development department at The Christie. This is to make sure that your safety and rights are respected throughout the study. This study has been approved by North West – Haydock Research Ethics Committee, 24/NW/018, committee meeting date 11/06/2024.

A previous version of this patient information sheet and informed consent was reviewed by patients and their family and friends. We have provided a single page visual overview of the study.

Thank you for considering entry into this study, your involvement helps us with future cancer treatment. Should you decide to take part in the study, you will be given a copy of the information sheet and a signed consent form to keep.

EGG-CUP

ENABLING GENOMIC TESTING IN CANCER OF UNKNOWN PRIMARY (EGG-CUP)

Participant Identification Number:	

1	I confirm that I have read the information sheet dated 07 August 2024 (version 1.2) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. please provide responses	
2	I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	
3	I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from <Insert participating site name>, from regulatory authorities or from The Christie NHS Foundation Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
4	I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers.	
5	I agree to my General Practitioner being involved in the study, including any necessary exchange of information about me between my GP and the research team.	
6	I agree to provide blood samples (as explained in the information sheet) for genetic testing.	
7	I agree to the collection of tissue from my previous biopsy/resection, and consent to these samples being used in research associated with this study.	
8	I agree to The Christie NHS Foundation Trust receiving additional genetic data from Foundation Medicine, which The Christie NHS Foundation Trust may use for research as part of this study or in future research.	
9	I understand I will be given results about any genetic abnormalities that have direct relevance for the management of my cancer.	
10	I understand this research may include a range of tests (other than genetic analysis) on my donated samples if relevant to the study. This may include sharing of samples with collaborators within and outside of the UK/European Union where data protection may not be as stringent as the UK. I understand my personal data will not be shared unless a diagnostic test is being performed which may require this information to be disclosed.	

11	Do you want to be told about results that may have significance for your biological family members (initial next to your preferred option)	
	Yes, I do want to be told	
	No, I do not want to be told	
12	Do you want to be told about results that are not related to your cancer but may have potential medical impact on you (initial next to your preferred option)	
	Yes, I do want to be told	
	No, I do not want to be told	
13	At the end of the study, I agree that my unused tissue and blood samples can be gifted for future research according to their strict policies and ethical approvals. I understand future uses may include genetic or pharmaceutical research and my samples and anonymised data may be shared with collaborators across Europe and the World where data protection policies may be less stringent than the UK. No identifiable information such as name or contact details will be provided to these partners	
	Yes, I agree	
	No, I do not agree	
14	I agree that my anonymised genetic data may be shared on a public database which will help speed up discoveries that improve the ability to diagnose, treat and prevent cancer. I understand that my personal identifiable information will not be disclosed but information about my cancer, race, gender and treatments may be made available.	
15	I agree that my pseudo-anonymised data, such as scan reports and blood results, may be collected as part of this study	
16	I agree to take part in the above study	

Please initial box

Would you like to receive a summary of the study results? ☐ Yes ☐ No

If yes, please provide your contact details:

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Name of participant:	_____	**Name of researcher:**	_____
Signature of participant:	_____	**Signature of researcher:**	_____
Date:	_____	**Date:**	_____

Name of witness: _____

Signature of witness: _____

Date: _____

When completed:

- One copy to the participant
- Original signed ICF in the patient's medical notes
- Copy in the Investigator Site File