UNIVERSITY OF LEICESTER

DOORS-M study: Development of a blOOdtest for uteRine Sarcoma – Monitoring

Participant Information Sheet: University Hospitals of Leicester

Principal Investigator: Dr Esther Moss

Introduction

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. The information provided below will help you to understand why we are doing the study and what is involved should you agree to participate. Please take time to read the following information carefully and discuss it with others if you wish. Please feel free to ask any questions you may have.

What is the purpose of the research study?

Uterine sarcomas are a rare cancer that account for 3 in 100 of cancers arising from the uterus, or womb. They can be difficult to diagnose since they have many of the same symptoms and scan features as uterine fibroids, and biopsy from the womb lining (endometrium) only detects 1/3rd of cases.

At present there is no blood test that can be used to guide patients and their doctors in the follow-up of uterine sarcomas or to identify cancer recurrence earlier. Circulating tumour DNA (ctDNA) is fragments of cancer released from cancer cells that can be detected within the blood and can be used to diagnose and monitor cancers. The genetic profile of uterine sarcomas is complex, and designing a ctDNA-based blood test to detect and follow-up uterine sarcomas needs to take these complexities into account, and to ensure that there is a clear difference from the profile of fibroids.

This project aims to pilot the use of a ctDNA-based test to help monitor patients who have undergone treatment for a uterine sarcoma. We will recruit patients who have been diagnosed with a uterine sarcoma and are under follow-up to collect information from their diagnosis, including scan images (ultrasound/magnetic resonance imaging (MRI)/computer tomography (CT)/positron emission tomography (PET) scans), blood test results, and pathology analysis, including genetic analysis (whole genome sequencing) of the tumour. This information will be used, alongside in-depth genetic analysis of a piece of the tumour that was removed at surgery and samples from any biopsies, to help develop the blood test.

Patients who attend the University Hospitals of Leicester will have blood samples taken every 3 months, which will be analysed to test how well the developed blood test works, and if it is able to detect uterine sarcoma recurrence.

In addition, we will perform additional image analysis on the MRI and/or CT scan images using Artificial Intelligence (AI). This is a type of computer technology that can help expert radiology doctors analyse scan images in greater depth, identifying features on the scan that may not be detected clearly by the human eye to see if this can is better able to identify sarcomas compared to expert radiology doctors. We will compare how well expert doctors with and without the AI analysis of the scans are able to predict whether a mass within the womb is a sarcoma or not.

The study also aims to collect the opinions and experiences of patients taking part in the study as to the potential use and impact of a blood test to support uterine sarcoma patients in follow-up.

Why have I been invited to participate?

You have been invited to take part because you have previously undergone treatment for a uterine sarcoma within the previous 10 years.

Do I have to take part?

No, taking part in this study is voluntary. If you do not wish to take part, this will not affect the care you receive in any way. If you do decide to take part but later change your mind, you are free to withdraw at any time, without providing a reason by contacting the research team using the information provided at the end of this information sheet. If you do decide to take part, you will be asked to sign a consent form and you will be given a copy for your records.

What will happen to me if I take part?

If you agree to take part in the study you will be asked to sign a consent form. The researcher will ask questions about you either over the telephone or in-person including: your ethnicity, age, height, weight, body mass index (BMI), your medical and family history, and if you are experiencing any symptoms. This will take approximately 30 minutes. Additional information will be taken from your medical records, including information on your medical, family and surgical history, the type of sarcoma that you had and the pathology results. Information and images from any ultrasound, CT, MRI or PET scans that show the uterine sarcoma will also be collected.

Your original tumour biopsies will be reviewed by study team's pathologist who will provide a second opinion on the subtype of sarcoma that you were diagnosed with. If there is a difference of opinion on your diagnosis this will be fed back to your clinical care team. This is unlikely since sarcomas are usually reviewed by several expert pathologists as part of the Multi-Disciplinary Team (MDT) review of your case at the time of diagnosis.

A small piece of tumour taken at your original surgery/biopsy will be analysed in the laboratory to confirm the type of uterine sarcoma and may undergo genetic (DNA) analysis. A small piece will also be taken from any other biopsies you may have had, for example to diagnose cancer recurrence. If your tumour has undergone genetic sequencing through the NHS genomic medicine service, we will request the sequencing results.

You will be asked to give a blood sample (up to 20mls or 1.5 tablespoons) every 3 months, or each time you attend for a follow up appointment with the oncology team. If you are due to undergo chemotherapy treatment you will be asked for a blood sample before each cycle of chemotherapy. If you are having radiotherapy or surgery, you will be asked for a blood sample before and after your course of treatment.

At each follow-up visit you will be asked if you are having any important symptoms to be aware of, for example vaginal bleeding or pelvic pain, this should take approximately 15 minutes. The results of any investigations you have to see whether the cancer has returned and/or how the cancer has responded to the chemotherapy/radiotherapy/surgery will be recorded along with any treatment that you have been given for the uterine sarcoma. This will continue until you are discharged from follow up or the study finishes. The team will also obtain further information from your medical records through the NHS for up to ten years.

The blood tests will be analysed to try and identify genetic markers that can detect and/or predict uterine cancer recurrence.

You and your doctors will not be informed of the result of the blood test since this is a new test and we need to make sure that it is able to detect cancer cells before we start using it to guide patient care. However, if genetic analysis were to find a result that could impact on your clinical management, or that of your family, then the research team would contact your clinical team for further investigations or referral to the genetics team. For example, if you were found to carry a change in a gene such as the breast/ovarian cancer gene BRCA.

You may be invited to take part in an interview to discuss your experiences in the study and your views on the potential for a blood test to monitor uterine sarcomas. This will take approximately 1 hour and will take place over the telephone or online using Microsoft (MS) Teams. You do not have to answer a question if you do not wish to. The interview will be audio recorded before being given a code number or pseudonym – 'pseudonymised' or 'deidentified' so you will not be identifiable in any way. Your views and experiences will be compared with other women who are taking part in this study and will be used to help the research team understand the patient's perspective.

What will happen to my data?

Any research information we collect will be deidentified with a code number or pseudonym meaning it will be given a code number in place of your name.

Your deidentified research data will be entered onto the study database. The Study database is password protected and is owned and maintained by the University Hospitals of Leicester and the University of Leicester. Final data analysis will be conducted on servers owned and maintained by the University of Leicester.

A database containing identifiable information for the purpose of contacting participants will be held on the University Hospitals of Leicester server, and access will be limited to delegated members of the research team only. Paper copies of the study data will be retained in a secure office environment at the University Hospitals of Leicester.

Your study data will be kept for ten years after the study has ended, and with your consent your study data may be kept beyond this time and used in future ethically approved research. This could be commercial or non-commercial research. These researchers may be based in the UK or overseas.

What will happen to any samples that I provide during and after the research?

The samples that are collected in the study will be transferred to the University of Leicester for DNA and genetic analysis.

Your scan images will be reviewed by an expert radiologist at University Hospitals of Leicester and key images of your uterus (womb) transferred to University of Leicester for AI image analysis.

At the end of the study, with your permission, we would like to keep your remaining blood samples (in their deidentified form) for use in future ethically approved research, including genetic/DNA analysis. Any remaining biopsy samples will be returned to the hospital pathology department or destroyed. If you give us permission to retain your samples for future research, it is necessary to retain your consent form until the samples have been depleted or destroyed. This may be longer than ten years. Your data will not be shared with any external commercial companies outside of the agreed data analysis.

The Human Tissue Authority is the regulatory authority responsible for the oversight and inspections of human tissue storage in the UK after a study has concluded. We require your consent form to comply with the Human Tissue Authority to ensure we have obtained your permission to retain the samples beyond the life of this study. Your consent form will be stored independently from your deidentified samples to ensure your samples remain pseudonymous to researchers that may use them in the future.

Will I be reimbursed or receive any payment for participating?

For additional hospital visits to give a sample of blood only (not related to your ongoing hospital care) you will be reimbursed at the usual NHS mileage rate is 45p/mile to a maximum of £60 per visit.

You should be advised to keep your milage or original train/bus receipts and bring them to each additional visit. Additional visits can only be organised by the research team and confirmed the day before the appointment, to ensure that laboratory staff are available for blood processing.

What are the possible benefits of taking part?

It is unlikely that you will receive any direct benefit from taking part in this research study. However, we hope that the results of this research study could potentially benefit other patients with uterine sarcoma in the future.

What are the possible disadvantages and risks of taking part?

The main disadvantage of taking part is the time commitment involved for additional hospital visits to give a blood sample, if this does not coincide with a clinic appointment. While there are no significant risks or side effects from having the blood tests done, you might feel slight discomfort or experience minor bruising. Another occasional reaction is feeling faint or lightheaded during or after the blood test. The research team will ensure you are comfortable and at ease during blood collection, and they are fully prepared to manage such responses promptly and appropriately if they occur.

If you take part in an interview, the questions may touch on sensitive topics, such as memories of your diagnosis or thoughts about your future health. The researchers are highly experienced in conducting these conversations with care, offering support, and guiding you to additional resources if needed, to help ensure your comfort throughout.

What if something goes wrong?

It is very unlikely that you would be harmed by taking part in this type of research study. However, if you wish to complain or have any concerns about the way you have been approached or treated in connection with the study, you should ask to speak to the gynaecology research nurses on 07929 838393, or contact Dr Esther Moss on leicesterGCRG@le.ac.uk who will do their best to answer your questions.

If you remain unhappy and wish to address your concerns or complaints on a formal basis, you should contact Patient Advice and Liaison Service (PALS) at:

University Hospitals of Leicester (UHL) Patient Advice and Liaison Services (PALS)
pals@uhl-tr.nhs.uk
0808 178 8337

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation but you may have to pay your legal costs.

The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

Will my participation be kept confidential?

While you are taking part in the study, your contact details will be made available to the researchers at the University of Leicester so that they can contact you to arrange the details of your research study appointments – no other personal detail will be shared with the University. On the consent form, you can also choose to be informed about the results of the study. If you consent for this to happen, we will store your contact details securely, separately from your research data, and we will only use them for the purposes you have chosen. Your contact details will be destroyed once they have been used for the purpose that you have agreed to.

You should also be aware that we have a professional and ethical duty to act on concerns for your safety and welfare. If we identify welfare issues, such as deteriorating illness or concerns of abuse, we may need to report these to your GP, your hospital team, or social services. We will tell you if we do this.

Your medical records and/or data may be accessed by authorised individuals from the Sponsor, regulatory authorities and the host NHS organisation for monitoring and audit purposes.

With your permission we may share your research data and/or samples with other academic or commercial organisations. These may be inside or outside the UK where data protection laws may differ. However, the sharing of data and/or samples will require a contract between the University and the receiving organisation and part of that contract will require them to follow our instructions about how to look after your data and/or samples carefully. Any data and/or samples will be shared in a way that you cannot be identified by the recipient.

Interviews will be audio-recorded using an encrypted recorder or MS Teams' in-built recording capability, transcribed (written up) by members of the research team or professional transcribers with established data security and confidentiality agreements with the University of Leicester. The recording will be labelled with a unique code in place of your name. The recording will be deleted from the audio recorder/MS Teams platform as soon as it has been transferred to the University of Leicester secure server. It will be deleted from the server once the recording has been written up and analysed. Any identifying information within the recording will be removed when your interview is written up.

How will we use information about you?

We will need to use information from you, your medical records, and results of scans and NHS Genomic Service for this research study.

This information will include your;

- Name
- NHS number
- Date of birth
- Age
- Gender
- Ethnicity
- Medical history, including information about your uterine sarcoma diagnosis and treatment
- Contact details (telephone number, email address)
- Genetic data

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.

The University of Leicester is the Sponsor of this research and is responsible for looking after your information. We will share your information relating to this project with the following types of organisations;

- Universities

We will keep all information about you safe and secure by:

- Keeping electronic records on secure password protected servers
- Keeping paper records in secure offices with access limited to the research team
- Collecting the minimum amount of data possible to conduct the research

Using a code number in place of your name on all research data other than the consent form

International Transfers

We may share or provide access to data about you outside the UK for research related purposes to:

- Joining with other research groups who are working on sarcoma to increase the number of cases for analysis
- If additional testing on the tumour or blood samples not available in the UK is needed

If this happens, we will only share the data that is needed. We will also make sure you can't be identified from the data that is shared where possible. This may not be possible under certain circumstances – for instance, if you have a rare illness, it may still be possible to identify you. If your data is shared outside the UK, it will be with the following sorts of organisations:

- Universities who are also working on uterine sarcomas
- Companies who perform genetic/DNA analysis of tumour/blood

We will make sure your data is protected. Anyone who accesses your data outside the UK must do what we tell them so that your data has a similar level of protection as it does under UK law.

We will make sure your data is safe outside the UK by doing the following:

- some of the countries your data may be shared with have an adequacy decision in place. This means that we know their laws offer a similar level of protection to data protection laws in the UK
- we use specific contracts approved for use in the UK which give personal data the same level of protection it has in the UK. For further details visit the Information Commissioner's Office (ICO) website: https://ico.org.uk/for-organisations/uk-gdpr-guidance-and-resources/international-transfers/
- we do not allow those who access your data outside the UK to use it for anything other than what our written contract with them says
- we need other organisations to have appropriate security measures to protect your data which are consistent with the data security and confidentiality obligations we have. This includes having appropriate measures to protect your data against accidental loss and unauthorised access, use, changes or sharing
- we have procedures in place to deal with any suspected personal data breach. We will tell you and applicable regulators when there has been a breach of your personal data when this is legally required. For further details about UK breach reporting rules visit the Information Commissioner's Office (ICO) website: https://ico.org.uk/for-organisations/report-a-breach

How will we use information about you after the study ends?

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

We will keep your study data for the minimum period of time required by University Policy (6 years). The data will then be fully anonymised and securely archived or destroyed.

What are your choices about how your information is used?

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. 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 wish to withdraw, please contact the study investigators to inform them of your decision.

If you choose to stop taking part in the study, we would like to continue collecting information about your health from your NHS records for up to 2 years. If you do not want this to happen, tell us and we will stop.

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. Also, we would like to continue collecting information about your health from your NHS records for up to 2 years after the end of the study. Please let us know if you do not want this to happen.

Where can you find out more about how your information is used?

You can find out more about how the University of Leicester uses your information

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by contacting a member of the research team via the e-mail address or phone number listed on this participant information sheet
- by contacting the University's Data Protection Officer via email on dpo@le.ac.uk

If you have any further queries, or would like to raise an issue with the Sponsor of this study, please email rgosponsor@le.ac.uk.

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. With your permission, we will share your study data with other researchers and/or commercial companies. If we share your data, your code number will be removed which means that your data will be fully anonymous and you will not be able to be identifiable.

Who is organising and funding the research study?

Sponsorship and insurance for study design and management will be provided by the University of Leicester based in the United Kingdom. We will be using information from you in order to undertake this study. This means that we are responsible for looking after your information and using it properly.

This research is funded by The Eve Appeal, a UK-based charity that focuses on raising awareness and funding research for gynaecological cancers.

Who has reviewed the research study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee. This study has been reviewed and has been granted a favourable opinion by South Central - Berkshire B Research Ethics Committee. 'Favourable Opinion' means that the committee is satisfied that your rights will be respected, that any risks have been reduced to a minimum and balanced against possible benefits and that you have been given sufficient information on which to make an informed decision.

What will happen to the results of the research study?

The data collected as part of this study may be used, in part or in whole, for the writing of educational projects such as a Master's Degree or a PhD. The results will also be published in a medical journal(s) and presented at medical conferences/meetings.

Direct quotations from the interview may be used in the study outputs. These quotations will be deidentified (given a code number or pseudonym) so you will not be identifiable in any way.

If you would like us to send you a written report of the results then please indicate this on the consent form. We expect the results of this study to be available from 2028.

What should I do if I want to take part?

You will be asked to complete an Informed Consent Form and to opt-in to a variety of research options by placing your initials within the Yes or No boxes. This will confirm you understand how your data will be processed, protected and reviewed for research purposes'.

Contact for Further Information

If you have a question that you wish to direct to members of the research team, please contact: Esther Moss. University of Leicester, Robert Kilpatrick Building, University of Leicester, Leicester LE2 7LX. Tel: 0116 252 5827 Email: leicestergcrg@le.ac.uk

Thank you for taking the time to read this information and consider taking part in this research.