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Supplementary Information Sheet for Additional Research Biopsies

MISSION-Fumarate: A physiological study of the metabolism of fumarate in cancer using hyperpolarised ^{13}C magnetic resonance imaging

This information sheet is a supplementary document in combination with the Patient Information Sheet (Version 1.1, dated 20 May 2020) for the above-mentioned study. Please take time to read the main information sheet and this supplementary information sheet fully to understand the research being undertaken and what it will involve for you. Please ask us if there is anything that is unclear or if you would like more information about this document or the patient information sheet using the contact details at the end of this document.

This document outlines the process dealing with the **optional** additional research biopsies that we may want to take from your tumour or mass prior to and after treatment (if you are planned to have treatment). This is **optional** and will not affect you taking part in the rest of the study (e.g. MRI scan and Hyperpolarised injection).

If you are satisfied with the information provided and are happy to undertake these additional research biopsies, you will be asked to sign a consent form; a member of the research team will also sign it. You are free to change your mind about taking part even after you have signed the consent form.

Below gives information about why and how these additional research biopsies will happen.

What is the purpose of these additional research biopsies?
The purpose of these additional research biopsies taken from your tumour or mass is to analyse the samples and compare the results to what we see from your MRI scan. The samples will be analysed for, but not limited to; fumarate concentration (the chemical which you are injected with at your MRI scan) and malate (the chemical that fumarate is converted into in your body). The concentration of these chemicals seen in different parts of the biopsy samples will then be compared to the corresponding areas of seen on the MRI scan images to see if there are any similarities or differences between the two procedures.

Why have I been asked to have additional research biopsies?
Where possible, we aim to perform the research biopsy samples at the same time as the biopsy samples that are taken for your clinical needs. These could be at a routine appointment or during surgery (depending on what procedures you are due to have). We will ask if you are willing to allow researchers to either use the remaining tissue sample that is not required by the clinical team or take a small number of extra samples at the same time. You will need to sign the main consent form of this study if you are willing for this to happen. We aim to do this in the first instance to avoid you having to have multiple visits to the hospital in order to have biopsies performed.

However, there will be occasions where your clinical team do not need to perform clinical biopsies, the clinical biopsies do not align with the research MRI scans or you are not due to have surgery. On these

occasions, we would like to ask you if you would be willing to have these additional research biopsies as described in this information sheet.

Do I have to have additional research biopsies?
No, having these additional research biopsies is entirely voluntary. If you initially decide to undergo these, you are free to withdraw from this at any time, without giving a reason and without affecting your participation in the main part of the study (e.g. the MRI scans) which you are also free to withdraw from at any time. Withdrawal or refusal to participate will not in any way affect the standard or type of care you will receive from the clinical team who are looking after you.

What will happen if I chose to have these additional research biopsies*?*
If you chose to have these additional research biopsies and are not due to have a clinical biopsy, you will be booked an appointment at Addenbrooke's hospital to have these research biopsies taken within seven days of having your first research MRI scan. We will endeavour to undertake these on the same day as your imaging if possible. If you are due to have treatment for your tumour or mass (decided by your clinical team), we will invite you back for another **optional** research MRI scan (as described in the main Patient Information Sheet). This will be within one month of the first research MRI scan you had and after this we will offer you another research biopsy appointment within seven days of this scan.

During your appointment for these additional research biopsies, a suitably trained member of staff performing the procedure will discuss this with you and any problems you may face after the biopsy. Biopsies are performed routinely around the world and most people have no side effects or only minor side effects (see below section on risk and side effects).

The biopsy will involve passing a needle through a small incision in your skin and taking a small piece of tissue from your tumour or mass. You are likely to have an ultrasound in order to guide the needle into the correct position. This will be discussed with you prior to your appointment. You may have to have some blood tests prior to the biopsy procedure, which is the same as normal clinical practice for biopsies. This is to check you do not have an increased risk of bleeding. If you are taking any medication that may thin the blood, please inform the researcher and it will then be decided if it is safe for you to have this procedure. When you arrive at the hospital for your appointment, you will be asked to change into a hospital gown and then asked to lie on the ultrasound examination table. The area of the skin where the cut will be made is cleaned with antiseptic and some of your body may be covered in a sterile sheet. Your skin will be anaesthetised and then the biopsy needle will be inserted into the tumour or mass.

Most biopsies do not hurt, but the local anaesthetic used may sting to start with and will soon pass. You may be aware of the pressure sensation as the needle passes into the deeper tissue but this is usually well tolerated. Depending on the type of biopsy, the procedure may take over 30 minutes to complete, although, you will be in the department for a longer period of time to ensure you have no complications after the procedure.

Criteria that may exclude you from participating
These are mentioned in the main Patient Information Sheet.

What are the possible benefits of taking these additional research biopsies?
Where it is not possible to obtain the biopsies through the clinical appointments, we hope that these additional research biopsies will allow us to compare with the results seen in your research MRI scan and also then compare to patients that have also undertaken the same process. This could also help to predict which patients will respond to which treatments with more accuracy. These are unlikely to be of direct benefit to you from taking part.

Reimbursements
As discussed in the main Patient Information Sheet, you will not receive any payment for participating in this study; however, we can reimburse any reasonable expenses such as travel and parking costs incurred by your participation in the study.

What are the possible risks/side effects of having these additional research biopsies?
Discomfort and bruising may occur during and after biopsy, however most patients cope well with this. Pain relief will be available in the unlikely event that any discomfort becomes more severe. The most important side effects that you need to be aware of are:

- Bleeding which may occur at the site of biopsy and happens to 2 in 100 people (2%).
- For some biopsy procedures, blood in your urine may occur and happens to 1 in 100 people (1%) but often resolves itself.
- Infection under the skin, which happens to 1 in 100 people (1%).
- Infection on the skin surface where the needle passes through, this happens to 2 in 100 people (2%)
- Where biopsies are taken but the sample collected is so small that the tumour is missed or because the sample taken of the tumour is not representative of the whole tumour. This happens to 5 in 100 people (5%).

Should any of the above occur, the appropriate medical measures will be taken to correct the issue such as antibiotic treatment for infections or closure of bleeding areas. If any of these occur after you have left hospital, you should seek medical advice from your GP or through the contact details at the end of this document.

What happens after taking the research biopsies?
You will only be asked to have two of these additional research biopsies, one prior to treatment and one after starting treatment (if you are due to have treatment). After having these samples taken, they will be processed, stored and analysed appropriately and will be anonymised with your unique study identification code given in the main part of the study (e.g. research MRI scan) so that you cannot be identified directly. Analysis may include but is not limited to genetic testing and growing cells to perform further experiments that look at cell metabolism. This is to compare with results from other patients with your type of tumour or mass. After analysis is completed, the results will be compared by the research team with the images from the MRI scan and will then be destroyed in accordance with the Human Tissue Authority's Code of Practice. Analysis may involve sending these samples in anonymised fashion to third parties or commercial companies.

Who will have access to these results?
Any information collected during these research biopsies will be anonymised so as to not be identified as coming from you and will be subject to the usual rules for medical confidentiality. Only a limited number of staff undertaking the study will have access to these results.

What will happen if I do not want to have these additional research biopsies?
You can withdraw from having these biopsies at any time without explanation. This will not affect your participation in the main part of the study (e.g. research MRI scan) and will also not affect any investigations or examinations that you might have in the future in the course of your routine health care. We would like your permission to use the data (without any personal details attached) up to the time of your withdrawal.

What if there is a problem?
If you have concerns about any aspect of the biopsies, you should ask to speak to the researchers who will do their best to answer your questions (see contact details at the end of this information sheet).

If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. The Patient Advice and Liaison Service (PALS) are available by telephone on (01223) 216756 and email at pals@addenbrookes.nhs.uk, regarding any formal complaints about the study.

Are there compensation arrangements if something goes wrong?
In the unlikely event of something going wrong and your being harmed during the study, this is covered by NHS and professional indemnity insurance. Problems related to the study design are also covered by insurance taken out by the University of Cambridge.

How will we use information about you?
We will need to use information from you and your medical records for this research project.

This information will include your NHS number, name and contact details. 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 unique code number instead.

We will keep all information about you safe and secure.

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.

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.

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.

Where can you find out more about how your information is used?
You can find out more about how we use your information:

- At www.hra.nhs.uk/information-about-patients/
- For Cambridge University Hospitals NHS Foundation Trust, please visit: https://www.cuh.nhs.uk/corporate-information/about-us/our-responsibilities/looking-after-your-information, or email the Data Protection Officer at: gdpr.enquiries@addenbrookes.nhs.uk
- For University of Cambridge, please visit: https://www.medschl.cam.ac.uk/research/information-governance/, or email the Information Governance team at: researchgovernance@medschl.cam.ac.uk.

Keeping information for future research
Information about you that is collected during a research study may be kept securely to be used in future research in any disease area, including research looking at social and economic factors affecting health. This may include combining it with information about you held by other health or government organisations such as NHS Digital. Usually the information is combined together by matching information that has the same NHS number. Doing this makes maximum use of the information you have provided and allows researchers to discover more. Researchers may not be able to specify all the possible future uses of the information they keep. It could include providing the information to other researchers from NHS organisations, universities or companies developing new treatments or care. Wherever this happens it will be done under strict legal agreements. This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or to affect your care.

Who has reviewed the study?
All research in the NHS is looked at by an independent Research Ethics Committee to protect your safety, rights, well-being and dignity. This study has been reviewed and given a favourable opinion by Essex Research Ethics Committee.

Contact details for further information

All of your questions should have been answered but if you have any further questions, you can contact the study team during office hours (9am to 5pm) who can provide further information regarding the study.

Please also contact the study team in the event of the following occurring:

- if you suffer an illness or a possible study related injury
- if you feel different in any way
- if you are admitted to hospital for any reason
- if you are seen at a casualty/accident/emergency department for any reason.

Telephone: 01223 767926 (secure voicemail)
Email: radiology.research@addenbrookes.nhs.uk

Out of Hours
If you decide to participate in this study, in the event of an emergency out of office hours, please contact:

Your own GP practice's telephone number. If the practice is closed you will either be diverted to the out of hours surgery or a recorded message will provide further instructions to obtain help.

At any time

Failing to contact one of the above numbers at any time, please contact:

A&E department 01223 217118

For complaints

PALS (Patient Advice and Liaison Service):

Telephone 01223 216756
Email pals@addenbrookes.nhs.uk

Thank you for considering taking part in this study. If you require any further information, please do not hesitate to contact us, we will be pleased to help you in any way we can. A copy of the consent form will be provided for you.