Participant Information Leaflet
ProMOTE—EMI-137 Study (Stage 1)

Prostate Molecular Targeting to Enhance surgery using EMI-137

We would like to invite you to take part in a study called ProMOTE—EMI-137. This study aims to test a new way of being able to see prostate cancer cells during surgery. Before you decide whether to take part, it is important that you understand why the research is being done and what it would involve for you. Please take time to read this information, and discuss it with others if you wish. If you have any questions please ask a member of the research team who will be happy to discuss any aspect of the study with you.

What is the purpose of the ProMOTE—EMI-137 study?

This study aims to test whether a 'marker' called EMI-137 which is injected as a drug, makes it easier for surgeons to see prostate cancer cells during surgery.

EMI-137 binds to a type of prostate cancer cell that has a protein called 'c-Met' on its surface. EMI-137 is attached to a fluorescent dye which shines in the dark (and can bind to and highlight prostate cancer cells with 'c-Met' protein. This was shown to work in patients with colorectal cancer, but we don't know if it will work in patients with prostate cancer. The researchers think that being able to see cancer cells more clearly during surgery will help the surgeon to remove all of the cancer cells, which will help to stop the cancer coming back. It will also help to avoid unnecessarily removing normal cells, which would improve outcomes after the prostate is removed, particularly related to urinary leakage and sexual activity.

The researchers want to test whether EMI-137 can bind to and highlight only prostate cancer cells during surgery, without highlighting any other tissue, which doesn't have cancer. They also want to find out the best dose (130µg/kg or a lower dose) and time to give the drug to patients before surgery. The lower dose will be tested first at 2 hours before surgery, if it highlights the prostate cancer cells well, without highlighting healthy tissue, there will be no need to change the timing or test the higher dose in patients. The dose you are given will depend on whether the drug has already been tested in patients and what the results showed.

The study also aims to look at whether there are any specific changes within the genetic makeup of each cell (the DNA) that can cause them to become cancerous or spread. To answer this question, the researchers will perform genetic tests on the tissue samples taken at the time of diagnosis, and those taken during surgery. The results will help the researchers to understand the differences between normal and cancerous cells. The researchers hope to find out which changes in DNA lead to prostate cancer development and progression.

Why have I been asked to take part in the ProMOTE—EMI-137 study?

You have been asked to consider taking part because you have been diagnosed with prostate cancer and you have chosen to have surgery to remove your prostate. We plan to involve up to 20 patients like yourself in Stage 1 of this study.

Do I have to take part?

No, taking part in a research study is entirely voluntary. We will go through this patient information leaflet with you and answer any questions you might have. You can also talk to anyone else (e.g. family or GP) about your decision whether or not to take part. You do not have to decide straight away. If you decide to take part you are still free to withdraw at any time and without giving a reason. Whether you take part or not will not affect the standard of care you receive.

What will happen to me if I decide to take part?

You will be invited to attend an information appointment to discuss the study with a member of the research team. If you decide to take part in the study you will be asked to sign an informed consent form. You will also be asked to provide a blood sample, undergo a physical exam, vital signs assessment and have electrocardiogram (ECG) (recording test to monitor your heart activity).

You will be given EMI-137 drug via an injection. It takes some time for the drug to bind to prostate cancer cells, so you will be given the drug two to four hours before surgery. The surgery will be conducted as per routine NHS procedure using keyhole surgery and a special camera. The camera is used to identify the dye, as explained to you by your treating consultant. The prostate will be removed and biopsies from any tissues highlighted by the dye will be taken. These biopsies will be looked at by a doctor who studies diseased tissue (histopathologist) to find out whether they contain cancerous cells. If any cancerous cells are found outside of the prostate, we will discuss the results and the best course of action with you at your routine follow up visit.

You will be asked to provide urine samples before and after drug injection, during your stay in hospital for the operation, between discharge from hospital and the routine follow-up visit 1, and at the routine follow-up visit 2.

After surgery you will receive usual NHS care, including follow-up visits and regular Prostate Specific Antigen (PSA) tests. The research team will access and record your routine PSA result.

Will I have to attend any extra clinic visits?

All study follow up visits will be at the same time as routine clinical visits, and you will not have to attend any extra follow up visits as part of the study. The diagram on the next page shows the steps involved in this study.

Study Information Visit
Read ProMOTE Patient Information Leaflet and discuss with research team

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Sign informed consent form
Blood sample, physical exam, vital signs, ECG

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Pre-surgery visit (routine)

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Drug injection and surgery
EMI-137 injection 2-4 hours before surgery.
Prostate removed, biopsies taken from any highlighted tissue.
Overnight stay in hospital (or longer, if needed).
Provide urine sample before and after drug injection, and during stay in hospital.
Collect urine samples from catheter twice a day (morning and evening) between discharge from hospital and follow-up visit 1

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Follow up visit 1 (routine, 10-14 days after surgery)
Catheter removed.
Bring urine samples collected between discharge from hospital and follow-up visit 1.

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Follow up visit 2 (routine, 6 weeks after surgery)
Urine sample, blood sample, physical exam, vital signs, ECG

What are the possible disadvantages and risks in taking part?

The EMI-137 drug has already been tested in a Phase I study in 20 healthy volunteers and 15 patients with high suspicion of colorectal cancer. The study showed that a single injection of the drug at the highest dose (130µg/kg) used in our ProMOTE—EMI-137 study was well-tolerated and safe.

You will not need to stay in hospital any longer than usual, your surgery and schedule of follow up visits will be the same as standard NHS care. If you agree to take part in the trial, you will be asked to provide extra blood samples, have physical exam, vital signs assessment and ECG after you sign the informed consent form and again at the 6-week follow-up visit. You will be asked to provide urine samples at different times. You will also receive drug injection 2-4 hours before surgery, , The injection and the use of a cannula (thin tube used to administer medication) carry a small risk of infection and haematoma (a swelling containing blood). Providing blood samples carries a small risk of bruising, infection, and fainting.

The EMI-137 drug has a blue colour. You might experience temporary change to the colour of your skin and/or urine during the 24 hours (or longer) after you are given the drug. If you notice any side-effects you may contact your GP and/or the research team during office hours (details on page 5).

What are the potential benefits of taking part?

Participation in the study will not directly benefit you. The main benefit of you taking part will be the information that we can gather as a result. This may help us improve treatment options for men with high-risk prostate cancer in the future.

What happens if I want to stop taking part in the study?

You are free to decline to join the study and may withdraw at any time in the future. This will not affect any treatment you might receive, now or in the future. If you decide to withdraw, inform the person who gave you this information sheet, or the appropriate researcher as listed at the end of this leaflet. Any data and samples collected before withdrawal will remain part of the study unless you have specific objections.

In addition, the Investigator may discontinue a participant from the study at any time if it is considered necessary for any reason. This will not affect your treatment in any way.

What will happen to the samples I give?

Small tissue samples may be taken during your surgery for research in addition to those taken as part of normal diagnostic processes. This won't affect the routine assessment of your diagnostic pathology samples. These extra samples and your routine pathology samples (which will be stored in a pathology diagnostic archive) may be used in research.

Your tissue samples obtained during surgery will be used for research including genetic tests which will help the researchers to understand the differences between normal and cancerous cells.

Your DNA samples will be assigned a code and your data will be identifiable only by this number. The material given to researchers will not have information that identifies you. However, your DNA is unique to you so it can never be completely anonymous.

With your consent, your de-identified samples will be stored for use in future ethically approved research studies.

They will be used mainly by local researchers, but ethically approved research projects may take place working together with other hospitals, universities, non-profit institutions or commercial laboratories worldwide.

What will happen to my data?

Data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' The University of Oxford is the data controller and is responsible for looking after your information and using it properly.

We will be using information from you and your medical records, NHS Digital and other central NHS registries and will use the minimum personally-identifiable information possible. We will store the de-identified research data and any research documents with personal information, such as consent forms, securely at the University of Oxford for 10 years after the end of the study. We will keep any other identifiable information about you for less than three months after the study has finished. If you agree to your samples being used in future research, your consent form will be held until the samples have been depleted or destroyed or for 10 years, whichever is longer.

The Oxford University Hospitals NHS Foundation Trust will use your name, NHS number, home address, and contact details, to make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. They will keep identifiable information about you from this study for less than three months after the study has finished, other than what is retained in your medical records as per local Trust policy.

Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at:

http://www.admin.ox.ac.uk/councilsec/compliance/gdpr/individualrights/

You can find out more about how we use your information by contacting the study team on promote@nds.ox.ac.uk

What if something goes wrong?

The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. NHS indemnity operates in respect of the clinical treatment, which is provided. If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, please contact the trial team (promote@nds.ox.ac.uk), The Chief Investigator (Prof Freddie Hamdy, freddie.hamdy@nds.ox.ac.uk), or the University of Oxford Clinical Trials and Research Governance (CTRG) office (tel. 01865 616480 email ctrg@admin.ox.ac.uk).

The Patient Advisory Liaison Service (PALS) is a confidential NHS service that can provide you with support for any complaints or queries you may have regarding the care you receive as

an NHS patient. PALS is unable to provide information about this research study. The contact details for the Churchill Hospital PALS Office are Tel: 01865 235855 / Email: PALS@ouh.nhs.uk.

How will information about me be protected?

We will be using information from you and your medical records in order to undertake this study. Research is a task that we perform in the public interest. The University of Oxford, as sponsor, is the data controller. This means that we, as University of Oxford researchers, are responsible for looking after your information and using it properly. We will use the minimum personally-identifiable information possible.

Everyone who takes part in the study will be assigned a code number and all of the data relating to each person will be held on a computer database and will only be linked to that code number, and not to people's names or addresses. All samples relating to the study will only be labelled with the code number.

Responsible members of the University of Oxford, the Oxford University Hospitals NHS Foundation Trust and the regulatory authorities may be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations.

We will keep identifiable information about you for up to three months after the study has finished. We will store the anonymised research data and consent forms securely at the University of Oxford for ten years after the end of the study.

Oxford University Hospitals NHS Foundation Trust will use your personal information, including contact details and NHS number, to coordinate visits and obtain your health status for 6 weeks of follow-up. They will keep this information, held for research purposes, for up to three months after the study has ended.
If you agree to your samples being used anonymously in future research, your consent form will be held securely until the samples have been used up.

Your rights to access, change, or move your personal information may be limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate.
You can find out more about how we use your information by contacting the Surgical Research Team at srt@nds.ox.ac.uk .

Will my GP be informed of my participation in the study?

With your consent, we will notify your GP of your participation in the study.

Who is organising and funding the study?

The study is conducted by the University of Oxford, and funded by Cancer Research UK (CR-UK grant C1380/A18444). The researchers include a team of specialised doctors, scientists,

technical staff and nurses. Our team is experienced and has conducted similar research in the field.

What will happen to the results of this study?

Research findings will be used to confirm whether EMI-137 helps the surgeon to see prostate cancer cells and to decide whether a larger study should be carried out.

Any updates about the study will be added to the Surgical Intervention Trials Unit website (www.situ.ox.ac.uk) when they become available.

If a larger study is carried out, the results will be published in academic journals and presented at scientific conferences. It will not be possible to identify you from any report or publication placed in the public domain.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. This study has been reviewed and given favourable opinion by South Central - Berkshire Research Ethics Committee.

What if I have any other concerns? Who should I contact?

You will be given as much time as you feel you need to discuss any issues or questions involving this research during your appointment with the researchers and study nurses. If you have any cause to complain about any aspect of the way in which you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you and are not compromised in any way because you have taken part in a research study.

If you have any concerns or wish to discuss the study further, please contact one of the following:

Surgical Research Team, Email: srt@nds.ox.ac.uk, Tel: 01865 235944 or 01865 235943

Prof Freddie Hamdy, Chief Investigator, Email: freddie.hamdy@nds.ox.ac.uk, Tel: 01865 617123

Thank you for considering taking part.