Circulating tumour cells as biomarkers to predict prostate cancer metastasis for treatment stratification of localised cancer (C-ProMeta-1) Patient Information Sheet

Introduction

Many prostate cancer (PCa) cases diagnosed at early stage are indolent, meaning that immediate treatment, that have unwanted side effects, is unnecessary. However, some cancers are aggressive even when they are still small and confined within the prostate organ (localised PCa). If the cancer spreads outside of the prostate to other organs (called metastasis), it is very difficult to cure. Localised PCa is treated by complete surgical removal to be cured and is done as soon as possible before they spread to the other organs.

Systems have been developed, based on prostate biopsy data, Prostate Specific Antigen (PSA) levels and cancer imaging results to guide treatment decision. However, these systems are imperfect. Moreover, determining which curative treatment will be most effective for individual patients with localised PCa is challenging and remains a major obstacle in improving patient management and is recognised as an unmet clinical need.

Cancer metastasis is the main cause of PCa death and determines the selection of therapeutic methods. Theoretically, localised PCa may be cured by complete surgical removal. However, many apparently localised PCa cases treated by surgery removal reoccur, indicating the presence of undetectable micro-metastasis at the time of surgery. These particular patients require additional treatment after surgery, usually with radiotherapy and hormone therapy. The major challenge in managing aggressive localised PCa is differentiating truly localised PCa from those with micro-metastatic disease, which cannot be cured by surgery alone. A test is required which can be performed before surgery to distinguish patients suitable for surgical removal of the cancer from those who would benefit from more extensive hormonal-, chemo- and/or radio-therapy. No current imaging test has the resolution to detect micro-metastases that may consist of just a few viable PCa cells.

Circulating tumour cells (CTCs) are cancer cells spread into the blood circulation and from where they further spread to the other body site to form metastasis. They can be detected at a very early stage of cancer development. We hypothesise that detection of CTCs provides an accurate indicator of cancer micro-metastasis and CTC gene expression may predict the potential of future metastasis development. We have established a promising CTC analysis method, by which we have detected CTCs in all patients with metastatic PCa and for the first time have demonstrated the value of using CTC analysis in predicting prostate biopsy outcome of aggressive PCa diagnosis in pre-biopsy patients. Our CTC results may reflect the existence of micro-metastasis and determine the treatment method better than the current imperfect systems in clinical use.

Therefore, a study with after surgery outcome follow-up over a long period (10 years) is required to confirm the value of this CTC analysis in determining micro- metastasis, i.e. predicting post-surgery cancer recurrence and future metastasis development. This will be collaborative study of clinicians and research scientists at University College of London Hospitals NHS Trust (UCLH) and Queen Mary University of London (QMUL), where the CTC analysis and its value for predicting cancer metastasis will be performed. The samples and data will be stored securely in the Robert Lane Tissue Bank (RLTB) at Barts Cancer Institute, Queen Mary University of London. The aim of the study is to provide evidence and data for using CTCs to guide therapeutic choice in the management of localised PCa- giving the best treatment as necessary and avoid unnecessary treatment and associated side effects.

Once you have an understanding of the way we work, we hope you will agree to allow us collect, use and store your blood sample and clinical information for the current study and potential future use in support of cancer research.

Why have I been chosen?

We are inviting individuals who have been diagnosed with prostate cancer and will undergo surgery in an effort to completely remove the cancer.

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What will be involved if I agree to take part?
The study clinical research fellow (CRF) will discuss with you the research that is been undertaken and how the blood donated and the relevant clinical information will be used to improve prostate cancer diagnosis and treatment.

Blood is taken as part of your routine clinical care. During this procedure, which is carried out by a trained phlebotomist, we may ask your permission to obtain an additional sample for research (20 ml which is about 4 teaspoons). The sample will be taken during your routine clinic visit and will not involve any additional visits.

We would like to retrieve information about your diagnosis and treatment to link the information gained through analyses of the blood sample. This is to identify trends that would provide further information on the disease status and treatment response of prostate cancer. This in turn will assist in identifying biological markers of diagnosis and predictive of treatment outcome and ultimately lead to development of individualised treatment.

With your agreement to link the information we will access medical notes which will contain your name, date of birth, NHS number, hospital number, sex, date of diagnosis, treatment provided, and treatment response.

You will be contacted at by the CRF or a staff member associated with the study for 10 years in order to gather information regarding your cancer status, your standard care, blood test results and further treatment after surgery (only the first additional treatment after surgery). We will contact you twice in the first year after your surgical operation and once a year thereafter.

In case further longer-term follow-up after the 10-year is required, we will collect your cancer progression data through accessing the GP and NHS digital records with further ethical approval.

Do I have to do this?
No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

If you withdraw from the study, no further samples will be stored. If you wish, the stored samples that have not already been used will be destroyed on written instruction from yourself. We are obliged to keep records of the samples that have been destroyed.

Will there be effects on my treatment if I do not want to take part?
No. Consent is voluntary and not taking part will not affect the treatment and care provided by the hospital

What if I change my mind; can I withdraw from the study at any time?
Yes. When given, your consent remains valid indefinitely. However, you can withdraw your consent at any time by sending us an email or a letter with your contact details to the address mention on this document. If your donated samples have not already been used for research purposes, they will be removed from storage and destroyed as well as data that have been collected and stored. You will be informed by mail when this has been done.

How do we store blood sample and derivatives?
Fresh blood samples will be transported in designated sample carriers to the research lab at room temperature in the same day when they are taken for blood components isolation and analysis. Blood sample derivatives will be stored at very cold temperatures to preserve them for long term use. One part of isolated cancer cells will be fixed on glass slide and stored in -20^{o}C freezer and the rest of the

derivatives will be stored in -80 ºC freezer to preserve the integrity of the material in a designated storage area in a secure facility. All storage facilities are regularly monitored and under the close supervision of our staff.

How do we identify patients, what do we do with the information and when is access to personal details permitted?

The clinical care team at UCLH will identify eligible patients scheduled for prostatectomy, who will be approached for informed consent using the consent forms specifically designed for this project for blood collection and future research.

After patients have consented, a unique ID is allocated in order to pseudo-anonymise the samples breaking the direct link with the patient (donor). Except for staff authorised, no one else will be able to link the ID directly to the personal data. We keep personal data to identify and to obtain clinical information and some instances for follow up samples through the UCLH NHS Trust database if necessary. We also use the link between samples and the donors' identity should the donor later withdraw consent. This enables us to recover and then destroy samples not already released for research. Personal information about donors' identity is held in a secure electronic database. Paper records are held in locked storage, accessible only by authorised members of the study and the tissue bank. The information will be held indefinitely provided there is continuous ethical approval for tissue bank. Where any information could identify you, the information will be held securely with strict arrangements about who can access the information. The information will only be used for the purpose of medical research. Only information of the patients who have consented will be kept securely in the tissue bank database. The database is accessible only to authorised staff only.

Queen Mary University of London is the sponsor for this study based in the United Kingdom and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. Queen Mary University of London will keep identifiable information about you indefinitely with your consent. You can find out more about how we use your information at http://www.arcs.qmul.ac.uk/media/arcs/policyzone/Privacy-Notice-for-Research-Participants.pdf

Your information could be used for research in any aspect of health or care, and could be combined with information about you from other sources held by researchers, the NHS or government. Where this information could identify you, the information will be held securely with strict arrangements about who can access the information. The information will only be used for the purpose of health and care research, or to contact you about future opportunities to participate in research. It will not be used to make decisions about future services available to you, such as insurance.

Queen Mary University of London will collect information about you for research from electronic patients records at UCLH NHS trust with authorisation provided by UCLH via a data sharing agreement and from your GP and local hospitals with approval from Confidentiality Advisory Group (CAG). We will use this information to identify and gather information about the developments and progress related to your cancer and to identify potential biomarkers which might be adapted to use in clinical setting to improve diagnosis and the treatment of prostate cancer.

When you agree to take part in this research study, the information about your health and care, anonymously, would be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

What information is stored?
The information stored will include the categories below.

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Name, Date of Birth, NHS number, Hospital number, Sex, Ethnicity, Diagnosis, cancer diagnosis images such as MRI, and PET/CT, Treatment allocated, Response to treatment.

Will my information be kept confidential?
Yes. Samples are allocated a unique code upon receipt by the tissue bank as the pseudo-anonymisation process. While this code provides a link to the donor's consent form and other donor-related information, this information is stored separately and securely. Only designated and authorised staff associated to the study and the tissue bank staff will have access to this information.

Who will have access to the sample donated?
The laboratory research team of this research project will access the sample for the planned research with only the unique ID, but without the patient and clinical data. The tissue bank team will have access to the sample for sample management & audit purposes.

What type of research will be undertaken?
We are identifying changes in the blood sample that could be used to tell how a tumour is going to behave and response to the surgical treatment. The aim is to use our research findings to make a more personalised treatment to patients based on the findings from their blood.

Will researchers carry out genetic tests on my tissue?
Yes. We may use a variety of molecular biological and histology techniques and may study specific genes in cancer cells isolated from the blood sample that changes during cancer progression. For this, DNA and RNA will be extracted from your samples.
We will not use the samples to test inherited diseases and for reproductive cloning.

What will happen to the results of the study?
You will not receive any individual results. Overall results of research may be published in scientific journals and/or discussed in scientific and medical conferences. Such publication will never include any personal information about the donors. Publications can be provided if you are interested.

What are the safeguards and who has reviewed the study?
The samples will be stored in designated freezer with temperature monitoring and data will be securely stored in designated folder in the tissue bank database which is only accessible with authorisation. This study and the RLTB are regulated by the Human Tissues Act 2004 and we are also subject to the disciplines of the General Data Protection Regulation (GDPR) and Data Protection act 2018 UK. Further, our activities are reviewed by a Research Ethics Committee (whose remit is to defend patients' interests generally). In our case, the London City & East Research Ethics Committee has approved our work and our procedures.

What are the possible benefits of taking part?
There are no material benefits, either financial or in relation to your standard of care. The results of this research is unlikely to benefit you directly. However, it may lead to identifying new tests or treatment and with further research may benefit urology patients in the future.

What are the possible disadvantages and risks of taking part?
Blood samples will be taken at the same time when you will have your routine blood test for your diagnostic or treatment. There will be minimum risk to you in donating blood. It may cause a little pain and can sometimes result in some bruising. However where possible we will try to minimise any risks or inconvenience to you.

Will anyone else be told about my participation?
We may collect your cancer treatment and progression data from your GP. In this case we will send a letter to your GP to inform them of your participation in this study.

Who is organising and funding the study?

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The study is funded by Prostate Cancer UK and is sponsored by Queen Mary University of London.

How do I give my consent?
Once you have reviewed this patient information sheet and have received satisfactory responses to any questions arising with a member of your clinical team/the research nurse, we invite you formally to record your consent by completing the accompanying consent form.

Who should I contact for further information?
If you require further information you can contact the research team or the tissue bank using the contact details below,

Research team email:
bci-cmetapro1@qmul.ac.uk

Robert Lane Tissue Bank (RLTB)
Centre for Biomarkers & Biotherapeutucs,
Barts Cancer Institute,
Queen Mary University of London,
Joseph Rotblat Building,
Charterhouse square,
London.
EC1M 6BQ
Tel: 020 7882 3739

What if I have a complaint?
If there are any concerns on how we have approached or treated you during the process please contact our principal investigators Prof Yong-Jie Lu, Centre for Biomarker and Biotherapeutics, Barts Cancer Institute, Joseph Rotblat Building, Charterhouse square, London. EC1M 6BQ. Email: y.j.lu@qmul.ac.uk, Tel: 0202 7882 3597; or Mr Greg Shaw, Institute of Urology, University College London Hospitals NHS Trust. Email: gregshaw@nhs.net

If you have any concerns regarding how we process your personal data you can contact our information governance team on BCC-ISMT@qmul.ac.uk or the Information Commissioner's Office (ICO) https://ico.org.uk/concerns/handling/