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REASURE (Radium-223: Evaluation of Activity and SUrrogate REsponse)

A phase II open label study of biomarkers to assess response to radium-223 in patients with metastatic castration-resistant prostate cancer

PATIENT INFORMATION SHEET
Version 4.0, 22/02/2016

We are inviting you to take part in a research study called REASURE. Before you decide whether to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish. Ask us if there is anything that is not clear or if you would like more information. Please take as much time as you need to decide whether or not you wish to take part in the REASURE study.

Part 1 of this information sheet tells you about the purpose of the study and what taking part will involve for you.

Part 2 gives more detailed information about how the REASURE study will be run.

ICR The Institute of Cancer Research

The ROYAL MARSDEN NHS Foundation Trust

PART ONE

What is the purpose of the REASURE study?

We are looking at a treatment called radium-223 for men who have prostate cancer that has spread to the bones and has stopped responding to hormone therapy.

Radium-223 prolongs survival and improves quality of life in men with this type of cancer. However, it can be difficult to assess how well treatment with radium-223 is working for an individual. This is because the tests we currently use to measure cancer in the bone, such as bone scans, do not show this very clearly. We want to look at new ways to assess how well a patient is responding to radium-223 so that we know early on if it is the right treatment for them. We also do not know whether the standard dose of radium-223 is the best dose. REASURE aims to find out if these new ways of assessing the early effects of radium-223 can pick up differences between two doses of radium-223.

Radium-223 may also benefit patients with other types of cancer that tend to spread to the bone. The information we gain from this study might also help us to find the best way of using this new treatment in other types of cancers.

What is radium-223?

Radium-223 is a new type of internal radiotherapy treatment.

Radium-223 is similar to calcium and, like calcium, it is absorbed by active bone cells. Cancerous bone cells are more active than healthy bone cells and so are more likely to absorb the radium-223.

The radium is given by injection into the bloodstream and from there it circulates to the bones. The cancer cells in the bone absorb it. Radium-223 treatment uses a type of radiation called alpha particles to kill cancer cells. The alpha particles only travel a short distance, less than a millimetre. That means that the cancer cells receive a high dose of radiation but healthy cells, which are less likely to absorb the radium, receive only a low dose or no radiation at all. This leads to fewer side effects than some other types of radiotherapy.

The dose of radium-223 is measured in bequerels (Bq). The standard dose is 55Bq for every kilogram (kg) of bodyweight. In this study, some patients will receive 88kBq for every kg.

Why am I being invited to take part?

Your doctor believes you may be suitable to take part in this study because you have prostate cancer that is no longer responding to hormone treatment and has spread to your bones.

If you join the study, you will be one of about 40 men from across the UK taking part.

Do I have to take part?
No, it is up to you to decide whether or not to take part in REASURE. **If you decide to take part you are free to stop taking the study treatment or leave the study at any time. You do not have to give a reason.** Whether or not you decide to join the REASURE study will not affect the standard of care you receive.

What will happen to me if I decide to take part?
If you agree to take part in REASURE you will be given this information sheet to keep and asked to sign a consent form. You will need to have a number of examinations before you can join the study. Some of these are routine, but others will need to be done to check your suitability for the study.

What tests will be performed to see if I am suitable for the study?
You will be asked to answer some health questions and you will undergo different screening assessments to check your suitability for REASURE. These tests will be performed in hospital. They may all be done together during one visit, or across a few different visits. Your doctor will talk to you about this.

Your doctor or nurse will record your complete medical history, any treatments you have had for prostate cancer and any medications you are currently taking. They will also perform:

- a physical examination and measure your blood pressure and heart rate
- a Computerised Tomography scan (CT scan) of your chest, abdomen and pelvis
- a bone scan to map where your cancer is
- blood tests (about 20mls, or 4 teaspoons, in total) for routine safety checks and to measure your Prostate Specific Antigen (PSA) level and your testosterone level.

What if the tests show I'm not suitable for the study or I decide I don't want to take part?
Your doctor will discuss the alternatives to participating in this study with you.

What happens next if I am suitable for the study and decide to take part?
If, after the tests, your doctor thinks that you are suitable for REASURE and if you agree to continue in the study, you will be randomised (allocated) to one of two treatment dose groups. It is important that the patients in the two groups are as similar to each other as possible. This is because we need to be sure that if one group fares better than the other group, it is because of the treatment and not because the patients in the groups are different from each other in some way. The only way to make sure that the groups of patients are as similar as possible is to allocate them to a group at random (randomisation).

The two dose groups are:

1. 55kBq for every kg you weigh
2. 88kBq for every kg you weigh

Half of the patients in REASURE will receive 55kBq for every kg of weight and half of the patients will receive 88kBq for every kg of weight.

You will be asked to return to the clinic again within 2 weeks. At that visit, the study team will perform a few more assessments to collect some 'baseline' (i.e. before you start study treatment) information from you and to make sure it is still safe for you to take part. Your doctor or nurse will:

- conduct a physical examination including measuring your heart rate, blood pressure, weight and height
- obtain information about any disease-related symptoms you are experiencing
- obtain information about any changes to any medications you are taking
- take a blood sample to perform routine safety checks and to measure your PSA level.

Before you start study treatment you will also have 3 scans to measure where your cancer is:

- a diffusion-weighted MRI (DW-MRI) scan. DW-MRI is a new technique that gives us more information about your cancer than a routine MRI scan.
- two PET/CT scans using two different PET radioactive tracers. These two different PET/CT scans will be performed at least 12 hours apart. A PET/CT scan uses two forms of imaging at the same time:
  1) PET (Positron Emission Tomography) is a medical imaging technique in which a small amount of a radioactive tracer is given to the patient. This shows up any cancer cells and creates pictures of it.
  2) CT (Computerised Tomography) uses X-rays to produce images of the body.

By combining PET and CT we are able to collect important information about your cancer. In this study, we will perform two different types of PET/CT scans.

More information about the scans you will have as part of the study is given on pages 8-9 of this information sheet ('What do the research scans involve?').

You will be asked to give some extra samples as part of the research. We will use these to conduct laboratory research into your cancer. The samples we will request are:

- a blood sample. We will ask for approximately 35ml of blood, which is the equivalent of about 2 tablespoons. It is important that all patients donate this blood sample.
- a small urine sample. It is important that all patients donate this urine sample.
- a bone marrow biopsy. The bone marrow biopsy is an optional part of the study so you can still take part even if you do not want to give this sample.

More information about the samples you will be asked to give as part of the study is provided on pages 9-10 of this information sheet ('What sort of samples will I be asked to donate?').

You will receive your first treatment of radium-223 on the same day as some of the baseline assessments or on a different day. You will not have to stay in hospital overnight. This first series of assessments and treatment with radium-223 is called 'Cycle 1'.

You will receive radium-223 as an injection into a vein. Usually this is through a thin short tube (called a cannula) that is put into a vein in your arm each time you have treatment. This treatment should only take 1 minute to administer.

What happens after I have started treatment with radium-223?
You will have an injection of radium-223 every 4 weeks for up to 6 months (i.e. 6 'cycles' in total).

After 4 weeks you will have completed your first cycle of study treatment and will need to come back to clinic to start Cycle 2. Before administering your next treatment, your doctor or nurse will:

- perform a physical examination
- measure your pulse rate and blood pressure
- discuss whether you have experienced any side effects or changed any medications you are taking
- take some blood samples (approximately 40mls or 2 tablespoonfuls in total). These samples will be used for routine safety checks, to measure your PSA level and for research into your cancer
- ask you to provide a urine sample for research into your cancer. This sample should be given in the morning, after the first time you have completely emptied your bladder that day
- ask you to provide a bone marrow biopsy sample. This sample is an optional part of the study.

Within 2 weeks of this visit (either 1 week before or 1 after), you will also have:

- a DW-MRI scan
- 2 PET/CT scans

These scans cannot all be performed on the same day so you will need to make two or more separate visits to the hospital. Your doctor or nurse will arrange this with you in advance.

Every 4 weeks thereafter (i.e. at every cycle) you will attend the clinic to repeat the assessments you had at the 4-week visit. At each cycle you will be assessed for any side effects and will be asked whether you have taken any new medications.

After Cycle 2, the DW-MRI and PET/CT scans will be performed again at Cycle 4 and also at the end of study treatment. You will only be asked to provide a bone marrow biopsy a total of three times (all three of these are optional).

4 weeks after you receive your last study treatment, you will need to come back to the clinic. This is called the 'End of Treatment' visit. Your doctor or nurse will:

- perform a physical examination
- measure your heart rate and blood pressure
- discuss whether you have experienced any side effects
- take some blood samples (approximately 47.5mls or 2 tablespoonfuls in total). These samples will be used for routine safety checks, to measure your PSA level and for research into your cancer

- ask you to provide a urine sample for research into your cancer. This sample should be given in the morning, after the first time you have completely emptied your bladder that day.
- ask you to provide a bone marrow biopsy sample. This sample is an optional part of the study.

Within 2 weeks of the End of Treatment visit (either 1 week before or 1 after), you will also have:

- a DW-MRI scan
- two PET/CT scans

These scans cannot all be performed on the same day so you will need to make two or more separate visits to the hospital.

How long will I need to take radium-223?

Patients will receive treatment with radium-223 for six months. However, study treatment will be stopped before that if your study doctor finds that it is no longer helping to control your disease, you are experiencing unacceptable side effects or you no longer want to continue on the treatment.

Follow-up

Once you have finished your last cycle of treatment, your doctor will continue to check how you are. After your End of Treatment visit, they will assess you every four months until 1 year after your last treatment with radium-223. You will need to come back into clinic for each of these follow-up assessments.

At each follow-up, your doctor or nurse will:

- assess your health and physical performance status
- assess whether you have experienced any side effects that may be related to you taking radium-223
- record any other treatments you have received for your cancer
- take some blood samples (approximately 20mls or 1 tablespoon in total). These samples will be used for routine safety checks and to measure your PSA level.

Assessment schedule

The table below shows what will happen during the study. All assessments may be done over more than one visit:

	Before you start treatment	Cycle 1: Start of treatment	Cycle 2: 4 weeks after starting treatment	Every 4 weeks thereafter				End of treatment: 4 weeks after last treatment	4 months after last treatment and every 4 months thereafter for 1 year
				Cycle 3	Cycle 4	Cycle 5	Cycle 6		
A physical examination, including measurement of your heart rate, blood pressure and weight	X	X	X	X	X	X	X	X	
Blood tests for safety assessments	X	X	X	X	X	X	X	X	X
Assessment of health/physical performance status	X	X	X	X	X	X	X	X	X
Assessment of current symptoms and medications	X	X	X	X	X	X	X	X	X
Blood test to measure PSA level	X	X	X	X	X	X	X	X	X
Blood test to measure testosterone level	X								
Bone scan	X								
CT scan	X								
Collection of existing tissue sample for biological study		X							
Collection of blood samples for biological study		X	X	X	X	X	X	X	
Collection of urine sample for biological study		X	X	X	X	X	X	X	
Bone marrow biopsy (optional)		X	X					X	
Diffusion weighted MRI (DW-MRI)		X	X		X			X	
PET/CT scans (18F-fluoride and 18F-choline)		X	X		X			X	
Injection of radium-223		X	X	X	X	X	X		

What are the side effects of radium-223?

As with any anti-cancer treatment, radium-223 can have side effects.

The side effects of radium-223 that have been reported in previous studies are listed below. Most side effects are mild to moderate. **Not all patients will experience side effects.**

Very common side effects (these affect 1 or more men in every 10 treated with radium-223):

- diarrhoea
- low platelet count (platelets are colourless blood cells that are involved in clotting. A low platelet count may mean you bleed or bruise more easily).

Common side effects (these affect between 1 to 9 men in 100 treated with radium-223):

- low white blood cell count (this could make you more susceptible to infection).

Everyone in this study will receive regular check-ups to look out for the common side effects listed above, and any other problems, so they can be treated. Please let your study doctor know about any side effects as soon as possible so they can advise you what to do. This may include delaying your next treatment for a few days or stopping it completely. However, your doctor will talk to you before they make any changes to your treatment regime. Their telephone number is at the end of this information sheet.

What do the scans involve?

Computed Tomography (CT)

A CT scan uses special x-ray equipment to take pictures of the inside of your body to assess the extent of the cancer. It involves you lying down and keeping still on the scanner table for about 20 minutes. Usually, an intravenous agent is injected into your vein to obtain clearer pictures and you may also have to drink an oral contrast agent as well. You may experience some slight discomfort related to lying still while the CT scan is being carried out.

Bone scan

A bone scan uses bone-seeking radioactive material that is injected into a vein so it travels through the bloodstream. The radioactive material collects in the bones, in particular in areas where there is cancer. You then lie on a bed so a camera can take images of your bones. The dose of radioactive material is safe, and virtually disappears from your body within 24 hours.

The CT and bone scan are standard imaging techniques that will help your doctor to understand the extent of your cancer before you start treatment. If you were not taking part in this study, you would probably have undergone a CT scan and bone scan as part of your standard care.

Diffusion-weighted MRI (DW-MRI)

DW-MRI is a special form of scan that will provide extra information regarding your tumour which cannot be achieved using other imaging techniques. One of the most important aims of this study is to see if DW-MRI provides a better way of studying prostate cancer that has spread to the bones and evaluating how well the treatment is working.

These scans are similar to the standard MRI scans that are routinely used in clinical practice. To obtain MRI images, you will be asked to lie in a tube-like scanner, which uses a magnetic field linked to a computer to create pictures of an area inside the body. In order to assess the spread of the cancer, we will obtain images of most of your body. The DW-MRI scan will last about 50

minutes to an hour.

PET/CT

We will perform two different types of PET/CT scan in this study, which will allow us to collect more detailed information about your cancer and evaluate how well the treatment is working.

18F-Fluoride PET/CT

A PET/CT scan with sodium fluoride F18 injection is an imaging technique that scans your whole skeletal system and produces high quality images of the bones. These images can be used to detect areas of abnormal bone growth associated with tumours.

18F-Choline PET/CT

A PET/CT scan with 18F-Choline is an imaging technique that scans your whole body and produces high quality images. These images can be used to detect areas of increased cell activity associated with tumours.

In both types of PET/CT, you will have a small amount of radioactive tracer injected into a vein 1 hour before the scan. This helps to show up the sites of your cancer, including where it has spread to the bone. After the injection, you will be asked to lie down and rest quietly until the tracer has been absorbed by your body. Both types of scans will last for about 30 minutes.

You will be given full instructions on how to prepare for your scan before coming to the appointment so you know what to expect.

After the PET/CT scan, you can resume your normal activities straight away. You should feel no side effects after the procedure and no aftercare is necessary.

In total, you will have up to 12 additional scans (4 DW-MRIs and 8 PET/CTs) if you decide take part in REASURE. If you were not taking part in this study, you probably would not have a DW-MRI or PET/CT scan. These scans are being done to add to the information we learn as part of this research.

What sort of samples will I be asked to donate?

Within this study, research tests are being conducted to improve our understanding of the action of radium-223 on cancer cells and to find new ways of identifying how well cancer responds to this treatment. The samples that will be collected from you during the study will help us understand which patients to treat with radium in the future. A brief description of the different research samples to be collected is provided below:

Research blood tests

Blood samples will be taken at baseline, each time you receive radium-223 and at the end of treatment visit. Tumour cells and other substances found in blood will be looked at, as well as your DNA. We will take up to 35mls in total, which is about 2 tablespoons full, each time. Providing these blood samples is an important part of the study.

Tumour tissue

We will ask you to donate a sample of your cancer that has already been taken (for example, during investigations to diagnose your cancer or at another time prior to this study) and stored.

Bone marrow biopsy

You will be asked to consent to up to three bone marrow biopsies for research purposes. You can agree to have one, two or three biopsies performed, or none at all. The biopsy procedure will involve taking a small sample of your bone marrow using a special needle and this may be uncomfortable. In most cases the biopsy will be performed as a day case. You will receive a local anaesthetic before the start of the procedure to numb the area and Entonox ('laughing gas') throughout, to make it more comfortable. You may experience some pain, bruising or soreness as a result of the biopsy. There is a very small risk of infection or of bleeding at the site of biopsy and an even smaller risk of damage to structures that lie close to the entry path of the biopsy needle. Painkillers will be prescribed for you to take home with you if required. In most cases these side effects can be easily managed with simple measures and will resolve. Your doctor will explain in detail the procedure and the potential side effects to you.

Whilst these bone biopsies are optional, they are an important aspect of this study. The samples we collect will help us to further understand the effect of radium-223 on your cancer and identify specific features in the cancer that can predict responses to treatment. The tissue collected might help us in the future to predict which patients will benefit from radium-223 treatment.

Research urine test

Urine samples will be collected at several time points during the study to examine the effect of radium-223 on your cancer and on your bones. At each time point, the urine sample will be collected after you have completely emptied your bladder on the morning of your clinic visit.

What else do I have to do?

You will need to come to the hospital more often than you would if you were not taking part in this study. Before deciding whether to participate in REASURE, you need to carefully consider how the additional hospital visits and tests described in this information sheet will affect you and your family. Some tests may be uncomfortable. Please ask your hospital doctor or nurse if you have any questions about the tests and procedures.

If you decide to take part, you will need to:

- sign the study consent form to show you understand what REASURE involves.
- attend all scheduled appointments, including the scans. Some people may not feel like driving after having tests or receiving treatment. It is recommended that someone comes with you when you attend your hospital appointments.
- talk to your study doctor first if you want to stop receiving treatment with radium-223 for any reason.
- **tell your doctor about any other medicines that you take, even if you buy them without a prescription.** Before starting any new medication, including over the counter medications or herbal supplements, please check with your study doctor or nurse.
- tell your doctor about any medical problems or side effects you experience.

You will also be given a card, which will provide details about the REASURE study and that you are taking radium-223. Please carry it with you at all times while you are taking part in this study.

What precautions should I take if I choose to participate in this trial?
In general, the administration of radioactive medicines involves some potential risk to third parties. All patients receiving radium should follow good hygiene practices throughout the treatment and for at least one week after the last injection. This will minimise radiation exposure from bodily fluids to household members and caregivers. Radium-223 is excreted via the faeces and can be present in vomit. When you open your bowels, you should flush the toilet twice after each use. If any clothing comes into contact with faeces or vomit, it should be washed promptly and separately from other clothing.

Caregivers are advised to use suitable precautions, for example wearing gloves and hand washing, if they have contact with faeces or vomit from patients after they have received radium. Your doctor or nurse will be able to give you more information about this.

You should use double barrier contraception (e.g. condom plus spermicide in combination with a diaphragm, cervical cap or intrauterine device) during your radium-223 treatment and for 6 months following your last injection of radium-233.

What are the alternatives for treatment?
If you do not take part in this study, your doctor will discuss alternatives with you and you will be offered the best available alternative treatment.

What are the possible benefits of taking part?
Radium-223 might help to control the spread of cancer in your bones, but we cannot guarantee it. The information we gain from this study may help us to improve treatments in the future for patients with cancer that has spread to the bone.

What are the other possible disadvantages and risks of taking part?
You may experience some side effects which are not listed in this information sheet. There is no way of predicting if you will experience any, or how severe they will be. You must contact your hospital doctor if you experience any side effects or if you are not sure that any problems you may have are related to the treatment.

Taking part in this research study will involve several additional visits to the clinic. Being involved in any research study requires a level of commitment, such as regular clinic visits and additional tests. This may cause some disruption to your normal activities and home life and this should be discussed with your family and friends, if it will impact on them. We will be able to reimburse you for any extra travel expenses (please refer to the section 'Patient travel reimbursement' on page 16).

During this study, blood samples will be taken to perform a variety of tests. The number of blood tests required in this study is more than if you were receiving treatment outside of a research study. Risks linked with blood sampling include pain from the needle being inserted, light headedness, possible fainting and (rarely) infection.

We will try to minimise any possible risks, discomfort or inconveniences associated with the bone marrow biopsies performed in this study. You will have the opportunity to discuss what the procedure will involve and all the possible side effects with your study doctor before deciding whether to donate samples of your bone marrow.

Radium-223 is a radioactive substance and so contributes to your overall lifetime exposure to radiation. Exposure to radiation over a long time may be associated with an increased risk of cancer. The information gained from previous research studies suggests that the risk of this happening is very small. However, we do not yet have enough information to know if this would happen many years after patients stop receiving radium-223.

If you take part in this study you will have a CT scan before you start and also a bone scan. CT and bone scans use X-rays. X-rays can cause cell damage which may, after many years or decades, turn cancerous. However, for people taking part in REASURE the risk of this affecting them is very small. If you do not take part in this study, you will still receive both of these scans as part of your standard care.

As part of the study you will be required to have two different types of PET/CT scan, at four different times (a total of eight PET/CT scans). You would not have these scans if you were not taking part in the research. The eight PET/CT scan will expose you to an increased amount of radiation, which can cause cell damage and may be harmful in the long term. It is estimated that the lifetime risk of inducing a fatal cancer from this additional exposure is approximately 1 in 160. For comparison, the natural cancer mortality rate in the UK is 1 in 4. In view of your clinical condition the radiation exposure is not significant and the risk of long term harm is considered to be negligible.

You will also be required to have a DW-MRI scan four times during the study. Whenever possible, they will be done on the same day as one of the PET/CT scans. Although there is no X-ray exposure with MRI scans, the procedure involves you keeping still whilst lying down on the scanner table for the duration of the scan. You will be made as comfortable as possible before you start but it can be noisy and you will be in a narrower tunnel than for a CT. During the DW-MRI scan you may feel the scanner table vibrate. Some patients may feel claustrophobic and may experience discomfort related to lying still in an enclosed space for a prolonged period of time while the scan is being taken.

If you have private medical insurance you should check with the insurance company before agreeing to take part in this study to ensure that your participation will not affect your cover.

What happens when the research study stops?
When you stop taking radium-223, your doctor will discuss your next options for treatment with you.

Involvement of your General Practitioner/Family doctor
Your General Practitioner (GP) will be informed about your participation in the study. This will ensure that your GP knows you are taking radium-223 in the event of any potential side effects and/or drug interactions.

PART TWO – GENERAL INFORMATION ABOUT HOW THE REASURE STUDY WILL BE RUN

What will happen to any samples I give?
All samples collected as part of the REASURE study will be sent to specialist research laboratories where they will be stored securely. Expert scientists, working together with the REASURE study team, will look at the samples you provide. We are interested in using these samples to identify biological markers that could tell us how well radium-223 is working early on in your treatment. In the future, this could mean that doctors are better able to monitor how effective the therapy is and change it if it is not working.

We also hope to find biological markers that may help to predict how well radium-223 treatment will work for individuals. This will involve looking at the genetic information in the samples we collect from you and at any changes in response to treatment. You will not be provided with information from any of the tests conducted on your samples.

There is currently no information available to help doctors to individually select the best treatment for people with your type of cancer. The samples you donate will help to provide this information for doctors to use in the future. We may in the future share the information we gain from the samples you provide, including genetic details, with other researchers investigating this type of cancer. You will not be identifiable from this information. Please initial the consent form if you are happy for this information to be shared.

If you give your permission, after the REASURE study is complete, your samples will be stored for

use in future studies. Any research using your samples will have approval from a Research Ethics Committee. If you do not give your permission for this, any of your samples remaining at the end of the trial will be disposed of in accordance with relevant legislation.

Will my taking part in this study be kept confidential?

All information which is collected about you during the research will be kept strictly confidential. When you join the study, your name, date of birth, hospital number and NHS or Community Health Index (CHI) number will be passed to The Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU) where the study is being coordinated. You will be given a unique trial number, which will be used together with your initials and date of birth on information that the research staff will send to ICR-CTSU. All information about you will be stored securely. It will be treated as strictly confidential and nothing that might identify you will be revealed to any third party. Only members of the research team will have access to the information that could allow this study number to be linked to you.

Members of the research team, including ICR-CTSU and NHS Trust staff, Sponsor representatives, employees of the regulatory authority approving the trial, and Bayer (the pharmaceutical company that supply radium-223) may examine your medical records to ensure the study is being run properly and that the information collected on the forms is correct. However, your confidentiality will be protected at all times.

We will be contacting your hospital from time to time to find out how you are getting on. Ideally we would like to do this for life, but patients sometimes change address and/or GP or lose touch with their hospital. If this happens we would like to use national records, which are kept on everyone's health status, to find out how you are. One of these is held at the General Register Office (GRO). Any details we receive from any source are confidential and will only be used for the purposes of the study. Please initial the consent form to show that we have your permission to do this.

You will retain the right to ask to be shown all your personal data that has been collected for this study, and if you think anything is incorrect you may ask to have it corrected.

All the information that is sent to ICR-CTSU will be kept for at least 5 years after the REASURE study has ended.

Will information about me be shared with other researchers?

The organisers of this study would like to be able to combine information we collect about patients in REASURE with information collected for other studies, if in the future it is a useful way of advancing our knowledge of the treatment of cancer. If this happens, information about you may be passed to other researchers, but they would not be able to identify you from the information provided.

What happens if I don't want to carry on with the study?

You are free to withdraw from REASURE at any time. You do not have to give a reason and your future treatment will not be affected. Your doctor will discuss your treatment options with you and

will offer the most suitable treatment available. However, if you were to withdraw, we would like your permission to keep the information and samples we have already collected from you and to continue to collect information on your progress that is routinely recorded in your medical records. If you decide to withdraw completely and don't want us to use anything we have collected so far, you must inform your study doctor who will ensure that all data and any stored samples that can still be identified as yours are destroyed.

What if relevant new information becomes available?
Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your research doctor will tell you about it and discuss whether you want to, or should, continue in the study. If you decide not to carry on, your research doctor will make arrangements for your continued care. If you decide to continue in the study you may be asked to sign an updated consent form.

If new information means it would be in your best interests to withdraw you from the study, your doctor will explain the reasons and arrange for your continued care.

If the study is stopped for any other reason, you will be told why and your study doctor will arrange for your continued care.

What if something goes wrong?
Every care will be taken in the course of this clinical study. If you are not happy with the general care and treatment you receive during the study, please speak first to your study doctor, who will try to resolve the problem. If you remain unhappy and wish to complain formally about the care and treatment received during the study, you may do so under the standard NHS complaints procedure which is available to you from your study doctor's hospital.

If you suffer any side effects or injury, please notify the study doctor immediately so you can obtain appropriate medical attention.

In the unlikely event that you are injured by taking part, compensation may be available.

If you are harmed due to the negligence of someone treating you, then you may have grounds for legal action for compensation. NHS Trusts are responsible for clinical negligence and other negligent harm to individuals that are under their care and covered under the NHS Indemnity Scheme.

If you suffer adverse side effects of the study medication or harm caused by procedures you have undergone specifically for the study you may be able to claim compensation from The Institute of Cancer Research. In deciding the level of compensation to be awarded, consideration will be given to the likelihood of side effects and any warnings that were given.

Patient travel reimbursement

You will be reimbursed up to £60 per cycle as a contribution towards travel expenses incurred whilst attending the additional visits that will be required in the REASURE study. Please speak to your study doctor about this.

Who is organising and funding the research?

The research study is being organised by The Royal Marsden NHS Foundation Trust (Chief Investigator Dr Chris Parker) and The Institute of Cancer Research. It is being coordinated by The Institute of Cancer Research Clinical Trials & Statistics Unit. Bayer Healthcare Pharmaceuticals are supplying the radium-223 for free and are also providing funding to run REASURE. The funding helps to cover the cost of including you in the study, the scans and laboratory tests, and helps support the study staff. None of the researchers are personally benefiting from this grant.

Who has reviewed the study?

REASURE has been approved by a Research Ethics Committee called 'NRES Committee London – Surrey Borders'. Their approval means they are 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 the right information to decide whether to take part.

What will happen to the results of the research study?

Independent experts will review the progress of the research and the results will be published in a medical or scientific journal as soon as there is enough information to be sure the results are reliable. You will not be identified in any report or publication. The results will help to decide how to treat metastatic castration-resistant prostate cancer in the future.

What happens now?

Your doctor or nurse will be happy to answer any questions. Once you have reached your decision please let your doctor or nurse know. If you choose to join the REASURE study you will be asked to sign a consent form and will be given a copy to keep together with this information sheet.

Further information

Macmillan is a registered charity providing information, emotional support and publications about all aspects of cancer for cancer patients and their families. They have published useful booklets about: (1) prostate cancer; (2) individual treatments; and (3) clinical studies in general. You can contact one of their specialist cancer nurses on 0808 808 0000. You can learn more about clinical studies on the Cancer Research UK's patient website (www.cancerhelp.org.uk).

Thank you for your interest in our research.

Your specialist is: _____

Contact phone numbers: _____

REASURE Sub-study

If you agree to participate in REASURE, you may also be invited to take part in an optional sub-study.

The sub-study aims to assess the feasibility of using a new method to assess treatment response using information collected from PET/CT scans and blood samples. This part of the study is optional for patients and will not run at all centres.

What does taking part in the sub-study involve?
You will be asked to consent to two additional blood samples being taken at the same time as your 18F-Fluoride PET/CT scans.

If you decide to take part, you will have two samples of blood taken via a cannula at your first 18F-Fluoride PET/CT scan and two samples of blood taken at your 18F-Fluoride PET/CT scan at Cycle 4. Each time, the first sample will be taken before the scan (approximately 55 minutes after your radioactive injection), and the second sample will be taken after the scan through the same cannula.

The amount of radioactivity in the blood at these two time points will be measured and this information will be used to look at ways to improve accuracy in analysing PET/CT scan data. This sub-study could help us to improve how treatment response is measured.

If I want to be part of the REASURE study, do I have to take part in the sub-study?
No. Taking part in REASURE does not mean you have to take part in the sub-study.

This is an optional part of the study so you can still take part in the main REASURE study even if you do not want to give these extra samples.

If you are asked to join the sub-study and agree to take part, please sign the relevant statement on the consent form.