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**Research Trial of Treatments for Patients with Bony Metastatic Cancer of the Prostate. -
TRAPEZE**

Patient Information Sheet

Your doctor has explained to you that your prostate cancer is no longer responding to hormonal treatment. We would like to invite you to take part in a research study to treat you with chemotherapy. Before you decide *whether to take part* 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. Take time to decide whether or not you wish to take part.

Further information and a summary of the principles of clinical trials can be found on the Cancer Research UK's patient website (www.cancerhelp.org.uk) together with information about this trial.

Purpose of the Study

It is believed that chemotherapy may be beneficial in treating your prostate cancer. Chemotherapy is currently a standard treatment for prostate cancer that has spread to the bone. The main aim of this study is test the effects of combining two further known treatments for prostate cancer at different time points, with chemotherapy. The three treatments involved in this study are described below

Docetaxel (Taxotere®) is a chemotherapy drug and is approved in the UK for the treatment of advanced breast and lung cancer. Docetaxel (Taxotere®) has been approved for use within clinical trials for the treatment of prostate cancer. Recently published studies (including an international prostate cancer clinical trial study called Tax-327) demonstrate that Docetaxel (Taxotere) improves symptom control and survival times. Zoledronic acid (Zometa®) is a bone-strengthening agent approved in the UK for treating cancer affecting the bone.

Strontium-89 is a type of radiotherapy (given by an injection), which is also approved in the UK for treating cancer affecting the bone. Early studies show that it may provide additional pain relief when combined with chemotherapy and may improve your condition.

The aim of the study is to assess how effective and safe Zoledronic acid (Zometa) or Strontium-89 is in treating your disease when given in combination with chemotherapy.

Approximately 1240 patients with cancer no longer responding to hormone treatment will be asked to take part in this study. The study will be open to recruitment for up to 5 years. A patient enrolled onto this study will be expected to visit the hospital every 3 weeks for chemotherapy treatment for 32 weeks. After this period patients will be expected to attend the hospital on a regular basis for a maximum follow up period of 2 years. This trial may also be known under the

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shorter title of 'TRAPEZE', named after the treatments involved which include Taxotere®, Radioisotope and Zoledronic Acid (Zometa®).

Taking part in the Study

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. The original consent form will be stored by your hospital and a copy of the consent form will be sent to the coordinating centre.

If you decide to take part you are still free to withdraw at any time and without giving a reason. This will not affect the standard of care you receive.

Description of the Study

When we do not know which way of treating patients is best, we need to make comparisons. Everyone who agrees to take part in this study will be put into a treatment group.

The treatment you receive will be chosen by a process called randomisation, the treatment is randomly allocated by computer, which is like making a choice by tossing a coin. This means that you have an equal chance of being treated with one of the above treatments. You and your doctor will know which treatment you are receiving.

The Four treatment groups in this study are:

- A) Docetaxel
- B) Docetaxel + Zoledronic acid
- C) Docetaxel + Strontium-89
- D) Docetaxel + Zoledronic acid + Strontium-89

If you agree to take part, your doctor will perform a number of tests and examinations before and during and after the study. You will also be asked to complete a number of questionnaires. These are summarised below:

General medical and physical examinations

Blood tests

X-rays, CT and bone scans - To measure your cancer response to treatment

DXA Scan (Bone density scans) – To measure bone density

Pain diary

Quality of life questionnaires

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Docetaxel, Zoledronic acid and Strontium-89 are given by a drip into a vein in your arm. This is called an infusion. You will receive one of the following treatments:

- A)** Docetaxel 75 mg/m² as a one hour intravenous infusion every 3 weeks for a maximum of 10 cycles.
- B)** Docetaxel as a one hour intravenous infusion every 3 weeks for a maximum of 10 cycles with Zoledronic acid every 3 weeks. Zoledronic acid will then continue alone every 4 weeks until you or your doctor wishes to discontinue it.
- C)** Docetaxel as a one hour intravenous infusion every 3 weeks for a maximum of 10 cycles and one treatment of Strontium-89 given 28 days after the sixth dose of Docetaxel as a short intravenous injection. Cycles 7-10 will then follow after a 28 day recovery period.
- D)** Docetaxel as a one hour intravenous infusion every 3 weeks for a maximum of 10 cycles, followed by one treatment of Strontium-89 given 28 days after the sixth dose of Docetaxel as a short intravenous injection. Cycles 7-10 will then follow after a 28 day recovery period.. Zoledronic acid will be given every 3 weeks throughout the treatment. Zoledronic acid will then continue alone every 4 weeks until you or your doctor wishes to discontinue it.

You may receive less than 10 cycles of docetaxel chemotherapy cycles. The exact number of cycles that you will receive will be determined by your doctor after consultation with you.

As part of your main treatment you will also be given steroid tablets (Prednisolone) to take during your course of treatment with Docetaxel. In addition you will receive extra steroid tablets (dexamethasone) for a few days around each infusion of chemotherapy to decrease the potential side effects of Docetaxel (allergic reactions and fluid retention).

You will be required to visit the hospital every 3 weeks until the end of therapy. The duration of treatment will be up to 32 weeks.

After the end of treatment your doctor will see you every 3 months in order to assess the status of your disease.

The flow chart below explains the visits you will make to the hospital and at which time.

Restrictions

It is important that you inform your doctor of any changes in your health whether or not you think it is due to the treatment. You should also tell your doctor of any changes to your medicines, either those prescribed by your GP or those you buy at the chemist.

Other treatments available

Your doctor will discuss the different treatment options available to treat your disease.

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Flow chart of the tests and procedures that will be carried out during the study

Tests & Procedures	Before Start of Chemotherapy	Before each administration of Chemotherapy	After chemotherapy	Follow up (every month for 3 months then every 3 months there after)
Read information Sign consent	✓			
Scanning Procedures (CT scan, MRI scan, Bone scan and/or Ultrasound)	✓			✓ (as clinically indicated)
DXA Bone Density Scan	✓			✓ (One year after start of treatment)
Other current medication / side effect information collected	✓	✓	✓	✓ (30 days after last infusion)
Medical history information collected	✓			
Height measured	✓			
Weight and physical exam and vital signs	✓	✓	✓	✓
Blood tests including PSA	✓	✓	✓	✓
Pain and Quality of Life assessments	✓	✓	✓	✓

Potential Side Effects and Risks

As with all medicines of this type there may be some unwanted side effects. You should discuss these with your doctor. The more common side-effects are listed below; there may also be other side effects that we cannot predict. Other medicines will be given to make side effects less serious and less uncomfortable.

With **Docetaxel** you may experience nausea and/or vomiting, mouth irritation, diarrhoea, fatigue, a pins and needles sensation in your hands or feet, hair loss, changes in your skin and nails, muscular pain, decrease in blood cell counts, infection, and swelling due to fluid retention. Your blood pressure may also fall while the drug is being given, and this will be checked carefully. The infusion of Docetaxel may cause temporary local irritation and bruises if it is given into a small vein. All these side-effects have been experienced by some patients during previous studies and most of them are reversible. (The items underlined may not be reversible).

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With **Docetaxel + Zoledronic acid** you may experience the same effects as stated for Docetaxel above with a rise in temperature, and flu-like symptoms, consisting of fever and bone pain due to the Zoledronic acid. Zoledronic acid may also affect your kidney function. Blood samples will be taken prior to zoledronic acid infusion at every study visit to check that your kidney function has not been affected.

With **Docetaxel + Zoledronic Acid + Strontium-89** you may experience the same side effects as stated above for Docetaxel and Zoledronic acid. The addition of Strontium-89 to Docetaxel and Zoledronic acid may cause some bone pain lasting 36 to 72 hours following injection. This can usually be controlled by analgesics (pain killers). Strontium-89 can also affect your blood counts following injection; these will be monitored very closely with regular blood tests.

With **Docetaxel + strontium-89** the addition of Strontium-89 to Docetaxel may cause some bone pain lasting 36 to 72 hours following injection. This can usually be controlled by analgesics (pain killers). Strontium-89 can also affect your blood counts following injection; these will be monitored very closely with regular blood tests.

As with any chemotherapy it is possible that your treatment could cause problems to an unborn child. You must take full contraceptive precautions if there is any chance of you fathering a child during and for at least 2 months after the treatment. If you have a fever or bruising after receiving either of the drug combinations, **it is important that you contact your hospital doctor immediately**. If you have a fever your doctor will perform some blood tests and may prescribe antibiotics.

For more information about risks and side effects, ask your doctor.

You may require one extra bone scan more than you would if you were not taking part in the study. You may require one additional CT scan and will receive two additional bone density scans (DXA scans) more than you would receive if you were not taking part in the study. Any potential health risk associated with these or any of the above scans is considered to be low for a patient with your medical condition.

The radioactive strontium is intended to give a very high radiation dose to any parts of your bones that are involved in your cancer. The rest of your body gets a lower radiation dose and your doctor will explain possible side effects with you. Any potential health risk associated with the radiation is considered to be minimal for a patient with your medical condition.

If you have private medical insurance you may wish to consult your medical insurers before agreeing to take part in the study. This is to ensure that your participation will not affect your medical insurance cover.

What happens when the research study stops?

At the end of the research study or if you withdraw, your study doctor will assess your symptoms, discuss your options and prescribe appropriate treatment. Rarely companies sponsoring research studies may decide to stop the study before it has finished. If this happens, your study doctor will explain the reasons why and arrange appropriate care for you.

Potential Benefits

The use of chemotherapy may result in a decrease in pain, improvement in the quality of life and a delay in the progression of your disease and improved survival times. This may be further improved by combining chemotherapy with Zoledronic acid (Zometa®) and/ or Strontium-89.

The information we get from this trial may help us to treat other patients with cancer more effectively in future.

Looking at Blood Serum Samples

In addition to your routine blood tests we would also like to take additional blood samples from you during your regular study visits for additional analyses. . We would also like to monitor changes in protein levels in your blood during treatment to see if it can help us better predict treatment outcomes.

Your participation in this part of the study is optional and will not affect the treatment that you receive if you do not consent to providing additional blood samples for these additional tests and research.

Looking at Tissue samples

As part of the clinical trial we would like to be allowed to have access to samples of your tissue, which were taken as part of your routine care and disease diagnoses. These samples will have been collected by your hospital and stored in Paraffin fixed wax blocks. If you agree these samples will be collected and tested for the presence of a number of different chemicals known as biological markers by the Institute for Cancer Studies – The University of Birmingham and other collaborative centres.

Your participation in this part of the study is optional and will not affect the treatment that you receive if you do not consent to providing additional blood samples for these additional tests and research.

Your rights regarding Tissue/ Blood samples taken as part of this clinical study.

The results of the analysis of your individual samples will not routinely be given to you unless it is of clinical significance and of importance to your health. You will not benefit financially, if this research leads to the development of a new treatment or medical test. Any publications resulting from the collection of these tissue or blood samples will be made available to you if requested. Please note that your participation in this part of the study is optional and will not

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affect the treatment that you receive, if you do not consent to providing additional blood samples or for the research team to have access to your stored tissue samples detailed above.

New Information

Sometimes during a study new information becomes available about the treatment that is being studied. If this happens your study doctor will tell you about it and discuss with you whether or not you want to continue. If you decide to withdraw your study doctor will ensure that your care will continue. You may be asked, if you decide to continue in the study, to sign a new consent form.

Voluntary Participation and Discontinuation

Your participation in this study is voluntary. If you agree to take part and then change your mind and wish to withdraw you may do so at any time without this decision affecting your future care. If you decide not to take part your doctor will discuss your future care with you. Your legal rights will not be affected by your giving consent to participate.

At the end of the study your Doctor will discuss future treatment options. It is not anticipated that patients will be switched routinely to the alternative treatment in the study.

Confidentiality and Patient Rights

If you agree to take part in the study you will need to sign and date the Informed Consent Form attached. Your medical notes will need to be seen by authorised members of our research team so they can collect information needed for this research study and also to check that it is correct. Your unique registration number will be used to make sure you cannot be identified outside the trial. All information, which is collected, about you during the course of the research will be treated as strictly confidential. The confidentiality of your medical records will be respected at all times.

We will continue to contact your hospital in the future to find out how you are getting on. Ideally we would like to do this for life, but patients often change address or can lose touch with their hospital. If this happens we would still like to be able to collect important basic details (Full name, Date of Birth, Hospital Number and NHS Number). The Office for National Statistics (ONS) keeps records that can easily provide the information we need, so we would like your permission to ask ONS to pass on this information. Any information received in this way remains confidential and is used only for the purposes of that particular trial. Please initial the consent form to indicate you are happy for us to do this. The information that will be collected from ONS will relate only to the status of your disease and current health. The ONS system will not be used to collect information such as your home address.

Your GP will be informed, with your consent, that you wish to take part in a clinical study. Your GP may be asked to provide information from your records, which are required for the study.

Your legal rights will not be affected by agreeing to take part in or withdrawing from the study. You are free to withdraw from the study at any time without giving a reason. If you decide to

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withdraw from the study this will not affect the standard of your routine care in anyway. Your doctor will continue to treat you with the same level of care.

The Study has been reviewed and approved by the South West Multicentre Research Ethics Committee, one of 13 national Research Ethics Committees, has given its approval.

You will be informed of any significant new findings that occur during the study as this may change your decision to continue.

What if something goes wrong?

You will be closely monitored both during and after therapy and any side effects will be treated as appropriate.

If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you

Results of the Study

At the end of the study the information collected will be analysed and published in recognised medical journals. Your study doctor will be informed of any publications and will be able to supply a copy of these publications to you on request. The identity of the patients who took part in the study will remain confidential. Your doctor and study nurse will also be informed of any results throughout the duration of the study.

Organisation and funding of the study

The research study is being carried out by the Cancer Research UK Institute for Cancer Studies, at the University of Birmingham. The research is funded by grants from the the Health Technology Assessment (HTA) programme. (A governmental funding body which funds clinical research) and the following pharmaceutical companies, Sanofi-aventis and Novartis Pharmaceuticals Uk Ltd. During your involvement in this study no travel costs incurred by you or you family will be paid. Your doctor or any other members of staff that are involved in your treatment and care have not been paid for entering you into this clinical trial or receive payment for conducting the study.

Time to Consider

You should take at least 24 hours to decide if you wish to take part.

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Who Should You Contact with Questions?

You will be given a copy of this information sheet and the signed consent form to keep. If you have any problems or questions about this study or your rights as a patient in clinical research you should contact:

Doctor

Study Nurse

Tel No

Tel No

24 hour contact number:.....

The 24 hour contact number can be used out of working hours (9am – 5 pm) in the event where you need you contact a hospital doctor immediately.

We would like to thank you for reading the Patient information sheet and for considering taking part in this Clinical Trial. If you have any further questions please talk to the study doctor before considering entry into this clinical trial.