To be printed on local hospital headed paper

Radiotherapy with and without chemotherapy in the conservative treatment of muscle invasive bladder cancer

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You are being invited to take part in a bladder cancer research study. 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.

Consumers for Ethics in Research (CERES) publish a leaflet entitled 'Medical Research and You'. This leaflet gives more information about medical research and looks at some questions you may want to ask. A copy may be obtained from CERES, PO Box 1365, London N16 0BW. www.ceres.org.uk
A summary of the principles of clinical trials can be found on the Cancer Research UK's patient website (www.cancerhelp.org.uk). Information about this trial can also be found at www.bc2001.org.uk.

Thank you for reading about this study.

What is the purpose of the study?

Research suggests that giving chemotherapy (cancer killing drugs) and radiotherapy treatments at the same time *may* be better than giving radiotherapy alone for patients with bladder cancer like you. However, we do not know if it really is better than giving radiotherapy alone. Chemotherapy has been added to radiotherapy for cancer of the anus (the lowest part of the back passage) and has resulted in improved long term control of the disease. The way to find out if we can improve the treatment of bladder cancer is in a study, called a 'clinical trial'.

The purpose of this clinical trial is to see if giving chemotherapy and radiotherapy together is better than giving radiotherapy alone. Radiotherapy can sometimes cause side effects.

We want to measure the short and long term side effects of chemotherapy and radiotherapy. If you agree to take part in the study, you will be followed up at 3, 6, and 9 months after your usual treatment is completed and then annually.

Why have I been chosen?

Hospitals all over the UK will be taking part in this study. Approximately 350 patients like you who have been diagnosed with bladder cancer, will be included in this study. You have been chosen because your doctor feels that you are suitable for this study.

Do I have to take part?

Participation in this study is entirely voluntary. If you do decide to take part you will be asked to sign a consent form. You will be given a copy of this to keep together with this information sheet. 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.

What will happen to me if I take part?

When we do not know which way of treating patients is best, we need to make comparisons. Everyone who agrees to take part will be allocated a treatment group. It is important that the groups of patients are as similar to each other as possible. This is because we need to be sure that if one group fares better than another, it is because of the treatment and not because the groups differ in some way. The best way to make sure the groups are as similar as possible is to allocate patients to a treatment group at random (this means 'by chance' a bit like drawing lots and is done by computer which has no information about you, the individual).

The two treatment groups in this study are:

1. Standard radiotherapy (without chemotherapy)

2. Standard radiotherapy with chemotherapy

If you decide to take part in this study you will receive either standard radiotherapy with chemotherapy or standard radiotherapy alone. You will have an equal chance of receiving either treatment group.

The duration of your radiotherapy treatment will depend on your hospital's usual procedure and will be for either 4 weeks or 6 ½ weeks. If you are allocated chemotherapy, you will be given two different drugs: 5-Fluorouracil (5FU) and Mitomycin C.

What do I have to do?

If you agree to take part you will be asked to attend for your radiotherapy treatment just as you would if you were not taking part. If you are also allocated chemotherapy you will receive this whilst having radiotherapy. You will be given dietary advice to follow during radiotherapy and if you are receiving chemotherapy you should avoid unpasteurised dairy products. At the beginning of the study you will be asked to complete a questionnaire that assesses quality of life. This questionnaire should also be completed at the end of your treatment, at 3 months after the end of your treatment, at 9 months after the end of your treatment and at annual follow up visits for at least 5 years. These follow up visits are part of the standard care and there is no additional funding to reimburse travelling or other expenses.

You should refrain from donating blood during the study.

It is possible that if the treatment is given to a pregnant woman it will harm the unborn child. Pregnant women must not therefore take part in this study, neither should women who plan to become pregnant during the study. Women who are at risk of pregnancy may be asked to have a pregnancy test before taking part to exclude the possibility of pregnancy. Women who could become pregnant must use an effective contraceptive during the course of this study. Any woman who finds that she has become pregnant while taking part in the study should immediately tell her research doctor.

What is the drug or procedure being tested?

If you are given chemotherapy you will get 5-Fluorouracil (5FU) and Mitomycin C. The 5-FU will be given as a continuous infusion via a 'drip' in your arm into a vein for 5 days during the first week and 4th week of your radiotherapy. A single injection of Mitomycin C will be given on the first day of your radiotherapy.

You can receive your chemotherapy as an inpatient or as an outpatient. If your doctor decides that you may receive it as an outpatient a special tube called a 'PICC' line will be inserted into your arm before the treatment starts. A syringe containing the 5-FU drug is connected to a small automatic pump that will be attached to the tube in the hospital. The syringe is changed daily. You will be given a pouch to carry the syringe plus pump (about the size of a 'Walkman' cassette player) around with you.

Your radiotherapy treatment will be given in the hospital radiotherapy department. The treatment is usually given once a day from Monday to Friday with a rest over the weekend.

Radiotherapy has to be carefully planned. On your first visit, you will have a CT scan. The doctor uses it to work out where to give the treatment to kill the most cancer cells and miss as much healthy body tissue as possible. Marks will be made on your skin to be used to line up the radiotherapy machine every day when you have your treatment. After this you will be asked to re attend the radiotherapy department for a 'planning session'. You will be asked to lie under a large machine called a simulator. This takes normal x-rays. This is done to check the 'radiotherapy plan' is right for you and, in some cases, to take reference pictures of your treatment.

The actual treatment only takes a few minutes. Radiotherapy does not hurt and you will not be able to feel it. You will be alone while you have your treatment, but the radiographer will be able to hear and see you.

This planning process and treatment is the same whether or not you take part in the study.

What are the possible disadvantages and risks of taking part?

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 are the side effects of the treatments?

Patients who have undergone radiotherapy have experienced some or all of the following side effects to varying degrees: tiredness, diarrhoea, inflammation of the urinary bladder (cystitis) causing urinary frequency, bleeding, pain or discomfort on passing urine (dysuria), bloatedness and passing stools more frequently or with pain (proctitis). Most of these effects develop during the treatment and will improve after the treatment is completed. In a few patients, however, these effects can persist or can develop after treatment. Radiotherapy may also cause impotence in some men.

The side effects of 5-FU (chemotherapy) may include tiredness, diarrhoea, nausea (and rarely vomiting), mouth ulcers and a sore mouth (mucositis). Plantar-palmar syndrome is the redness and dryness of the skin of the hands and feet and is a rare side effect of chemotherapy. It is possible that the combination of radiotherapy and chemotherapy may result in both sets of side effects being worse, in particular the diarrhoea. Side effects associated with Mitomycin C include low blood counts and rarely it can affect the lungs (causing symptoms such as cough or shortness of breath). Hair loss only rarely occurs with this treatment.

You will be given advice about diet and, if necessary, tablets to control the diarrhoea. If you become unwell at home it is important to contact your own doctor or the hospital doctor.

Similar combined treatments are used for cancers of the anus and so we hope it will be possible to treat the bladder routinely without the side effects being too severe.

If you want more general information about chemotherapy or radiotherapy, please ask your specialist or research nurse.

Information on all aspects of cancer care is also available on the Cancer Research UK's patient website Cancer Help UK (www.cancerhelp.org.uk). Further information about the trial can be obtained from the trail website (www.bc2001.bham.ac.uk)

What are the possible benefits of taking part?

The combination of chemotherapy and radiotherapy has produced promising results in patients with other cancers and we are therefore hopeful that the treatment may be more effective in shrinking or stabilising your disease than radiotherapy alone.

We hope that a combination of chemotherapy and radiotherapy will help you. However, this cannot be guaranteed. The information we get from this study will help us to improve treatment for future patients with bladder cancer.

Looking at Bladder Tissue and Urine Samples

Bladder tissue is routinely removed when you have surgery and in later checks (biopsies) which are done as part of normal practice. When extra tissue is left over after your doctor has performed the necessary tests this is routinely stored in the hospital. Similarly, excess urine samples, which you will need to give for routine tests, are stored too. We would like to use these samples for research into bladder cancer. If you agree after the sample is removed it will be coded and personal details removed. The coding will maintain your confidentiality whilst allowing biological details to be compared to treatment findings. Please initial the consent form if you agree to this. If you do not agree you may still participate in the trial.

What are the alternatives?

The standard therapy for your disease is either radiotherapy alone or surgery to remove the whole bladder. Your doctor will discuss these therapies with you if you decide not to take part in the study.

What if new information becomes available?

Sometimes during the course of a research project, new information becomes available about the treatment or drug that is being studied. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw, your research doctor will make arrangements for your care to continue as normal. If you decide to continue in the study you may be asked to sign an updated consent form.

What happens at the end of the treatment?

Directly after you have finished your treatment you will be asked to complete a questionnaire on your quality of life. You will continue under the care of your oncologist and the urologist who will perform further cystoscopies (examination of the inside of the bladder using a telescope) to assess your response to treatment. This will happen at 3, 6 and 9 months after the end of treatment and thereafter at the discretion of your urologist but at least annually. This is part of the routine care for all patients receiving radiotherapy for bladder cancer. Further CT scans (CAT Scans) will be performed 1 year and 2 years after treatment is complete. At regular intervals after your treatment we will ask you some questions on possible side effects and on any problems you may be experiencing.

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.

What if I do not want to take part?
Participation in this trial is entirely voluntary. If you decide not to take part you do not need to give reasons for your decision and it will not affect your future treatment in any way. Your legal rights are not affected by participating in this study.

What happens if I change my mind during the study?
You are free to withdraw from the study 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 with you and will offer the most suitable treatment available. However, if you were to withdraw, we would like your permission to continue to collect information on your progress that is routinely recorded in your medical records. This is so that the overall quality of the study is not impaired.

Will my taking part in this study be kept confidential?
All information that 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. Information from your medical records, about your treatment and disease, will be sent to the BC2001 trial offices (Institute of Cancer Research and Cancer Research UK Institute for Cancer Studies). Your name will be passed to the trial offices when you join the study, after that a unique registration number will be used, together with your initials and hospital number, on all forms that the research staff send to the trial offices. Representatives from the trial offices and/or regulatory bodies may wish to see your hospital or clinic records to make sure the information sent was correct.

It is standard practice that your GP is notified that you are participating in a research study. We will ask your permission to do this before informing your GP.

We will be contacting your hospital over many years 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 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). We will need to give them enough information to identify you. This is usually your name, date of birth and NHS number (or Community Health Index and/or hospital number in Scotland). 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.

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 respected 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 bladder cancer in the future. Studies like these are often used in cancer research.

Who is organising and funding the research?
The research study is being carried out by the Institute of Cancer Research / Royal Marsden NHS Trust, Surrey in collaboration with the Cancer Research UK Institute for Cancer Studies, Birmingham. The research is approved and funded by the Cancer Research UK. The North West MREC, one of 13 national Research Ethics Committees, has given its approval.

Your doctor will not receive any payments for including you in this research study.

What do I have to do now?

You will have some time to think about the trial and make your decision. You may wish to discuss it with your family or friends. If, at any time, you have any questions about the study you should contact your consultant.

Local Consultants name:
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24-Hour Contact Number

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