For trial participants

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

A summary of the principles of clinical trials can be found on the Cancer Research UK's patient website, **Cancer Help (http://cancerhelp.cancerresearchuk.org/)** , together with information about this trial.

There is a patient information leaflet for the trial and a patient consent form. Your Doctor will explain to you how the treatment in the trial is suitable for you.

- **Download patient information leaflet (/Documents/college-mds/trials/crctu/bc2001/patient-info-sheet.pdf)** [pdf]
- **Download patient consent form (/Documents/college-mds/trials/crctu/bc2001/consent-form-v5.pdf)** [pdf]

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Aims of the trial

The study has been designed to test whether giving chemotherapy alongside radiotherapy can reduce the risk of cancer coming back compared to just giving radiotherapy alone.

Background to bladder cancer

Bladder Cancer

At the moment the best treatment for controlling bladder cancer remains to be determined. Bladder cancer may be controlled by surgical removal but in some patients the cancer may come back and further surgery will be needed. Bladder cancer can be treated without major surgery by giving radiotherapy to the whole bladder.

But this radiotherapy treatment can cause permanent shrinkage of the bladder and does not always control the cancer. This may result in half of the patients treated having surgery to remove the bladder, known as a salvage cystectomy. It is important to try and preserve the bladder as much as possible when treating the cancer as this will improve patients' quality of life.

Radiotherapy

Standard radiotherapy treatment involves giving radiotherapy to the whole bladder. However, it is not known whether it is necessary to treat the whole bladder or whether we can just treat the tumour alone. Results from other studies, including a large, randomised, controlled trial in prostate cancer, have shown that shielding normal tissue from radiotherapy can reduce late side effects. It is now necessary to test this reduced volume treatment in bladder cancer.

Chemotherapy combined with Radiotherapy Vs Radiotherapy Alone

Studies have been carried out on people with cancers found in other areas of the body (anal, head and neck, cervix cancer). These studies looked at the effectiveness and the side effects caused by giving chemotherapy combined with radiotherapy instead of just giving radiotherapy alone. Small studies in bladder cancer patients have shown that this combined chemoradiotherapy treatment has better results than those seen with radiotherapy alone.

However, these studies are too small and not enough patients were treated to see if the improvement seen would be true for all patients treated. It is now necessary to test this chemoradiotherapy treatment again in a large, randomised study. The chemotherapy drugs that will be combined with the radiotherapy in the BC2001 trial are 5-FU and mitomycin.

Eligibility and trial size

How many patients are involved?

The study will continue until there are at least 350 patients entered into one of two arms, either radiotherapy plus chemotherapy or radiotherapy alone. Radiotherapy can be given in one of two ways, either by standard radiotherapy or by whole bladder radiotherapy with tumour boost. With 350 patients, the trial will be able to detect reliably whether there is a difference between treatments and whether there is an improvement in survival.

Throughout the study the number of patients being entered to receive different treatments is monitored by an independent data monitoring committee. The committee will also look at side effects and make sure that patients are not experiencing severe side effects or that patients in one treatment group are not doing considerably worse than patients in another.

The first patient entered the study in August 2001

Who can enter the study?

Patients can enter the study if they:

- Are over 18 years
- Have been diagnosed with invasive bladder cancer that has not spread to the lymph nodes
- Have cancer which is localised within the bladder wall
- Are fit enough to have the treatment and are available for follow-up appointments
- Have adequate kidney, liver and blood tests
- Have given written informed consent
- If a patient has several separate cancers in the bladder (multiple tumours), they can still enter the trial, but will have to have standard radiotherapy treatment to the whole bladder (not the tumour boost treatment)

Who can't enter the study?

Some patients are not suitable to enter the study. This includes patients that:

- Are pregnant
- Have had any other cancer in the past 2 years, apart from basal cell skin cancer or carcinoma-in-situ of the cervix

- Have had inflammatory bowel disease (such as ulcerative colitis)
- Have had radiotherapy to the pelvis before
- Have had both hips replaced (this makes planning radiotherapy more difficult)
- Have had cancer spread to another part of the body (or to the lymph nodes)

Tests and examinations

Tests and assessments done before entering the study and starting treatment

All patients will have the following investigations before they can enter the study and receive treatment:

- Cystoscopy and tumour biopsy or resection with random biopsies of normal bladder mucosa
- Completion of bladder map
- Physical examination (including height, weight and surface area) to assess fitness and WHO performance status
- Full blood count (FBC), urea and electrolytes (U+Es), liver function tests (LFTS) to include Alkaline phosphatase, ALT or AST, bilirubin, albumin, calculated GFR by Cockcroft formula.
- MRI or CT of pelvis
- Chest X-Ray
- Bone scan and liver CT/US for raised ALP or AST
- *Assessment of bladder capacity.
- *Baseline RTOG toxicity, 'Lent Som' toxicity score. The Lent Som form will be completed by the doctor before the patient is randomised.
- *Quality of Life (FACT-BL Questionnaire) score will be recorded. The FACT-BL questionnaire will be completed by the patient before seeing the doctor.
- *Height, weight and surface area *
- Assessments carried out that are additional to standard practice

Randomisation procedure

After completion of the pre-treatment assessments and following discussion with the doctor and/or Nurse, the patient will choose whether to enter the study. If the patient chooses to enter the study they will provide written informed consent and can then be entered into the study.

Patients are entered through a randomisation procedure. This is where the patient's treatment is randomly selected by computer. There are two different treatment groups in the BC2001 study

- Synchronous (combined) 5-FU and Mitomycin with standard radiotherapy or whole bladder radiotherapy and tumour boost
- No chemotherapy and standard radiotherapy or whole bladder radiotherapy with tumour boost

If the doctor thinks that a patient should receive standard radiotherapy (i.e. the patient has multiple tumours) they can still be randomised to either chemotherapy or no chemotherapy.

Treatments

Treatment will last for either 4 or 6 1/2 weeks, depending on which is standard practice at the patient's hospital.

Synchronus chemotherapy

Treatment will last for either 4 or 6 1/2 weeks, depending on which is standard practice at the patient's hospital.

The chemotherapy (5-FU) will be given on weeks 1 and 4 of treatment, and the patient will wear a pump for a week at a time which will deliver a dose of 500mg/m2 /24 hours. Patients may have this treatment as an out patient.

Radiotherapy

Patients will first have a CT scan. This is so the doctor can see clearly the area to be treated with radiotherapy (planned treatment volume). Patients will be planned for treatment with an empty bladder and asked to empty their bladder 30 minutes before their scan.

Patients receiving whole bladder radiotherapy (standard radiotherapy) will receive the total radiation dose (55Gy in 20 fractions over 4 weeks or 64Gy in 32 fractions over 6.5 weeks, depending on hospital's standard practice) to the planned treatment volume.

In reduced volume radiotherapy treatment the volume of bladder irradiated is less than that in standard radiotherapy but patients will receive the same total dose as patients receiving standard radiotherapy. The CT scan is used to calculate the planned treatment volume, and radiotherapy is only given to the tumour volume with a 2cm margin.

Side effects

All treatments have side effects. You may only experience one or two side effects, or you may have more.

Radiotherapy

Applied to the Pelvic area can cause:

- Irritation of the bladder (cystitis)
- Diarrhoea
- Irritation of the back passage/ rectum (proctitis)

Radiotherapy can cause permanent side effects. Not everyone will have these side effects:

- Shrinkage of the bladder, causing frequent urination

- Sudden need to pass urine (urgency)
- Urge incontinence
- Diarrhoea
- Bleeding from the back passage (rectum) or blood in the urine

Chemotherapy

Chemotherapy also has side effects. Again, patients may only experience one or two of these effects, or they may have more.

5-FU is most likely to cause:

- Diarrhoea
- Sore mouth
- Red, peeling skin on hands and feet

Mitomycin is most likely to cause:

- Lowered blood cell counts, leading to increased risk of infection, bleeding and bruising

Hospital visits

The following schedule lists the times when patients will be required to come into hospital and the assessments they can expect to have.

During treatment

Patients should be seen weekly throughout treatment and the following assessments recorded:

- Full blood counts, urea and electrolytes
- Toxicity assessment by RTOG and CTC grading

Assessment at 9 months post randomisation

Physical examination

- Toxicity assessment by RTOG
- Chest X-Ray
- Cystoscopy (flexible or rigid)

At completion of treatment (planned or early)

- Physical examination
- Full blood counts, urea and electrolytes, liver function tests
- *Quality of life assessment by FACT-BL questionnaire (to be completed prior to consultation with Clinician)
- Toxicity assessment by RTOG and CTC

Annual assessment (QoL and Lent Som to year 5 only)

- Quality of life assessment by FACT-BL questionnaire (to be completed prior to consultation with Clinician)
- Physical examination
- *Toxicity assessment by RTOG and Lent Som
- Chest X-Ray
- Cystoscopy (flexible or rigid)

Assessment at 6 months post randomisation

- Physical examination
- Full blood counts, urea and electrolytes, liver function tests
- Toxicity assessment by RTOG
- *Toxicity assessment by Lent Som
- *Quality of life assessment by FACT-BL questionnaire (to be completed prior to consultation with Clinician)
- Chest X-Ray
- Rigid cystoscopy and cystoscopic biopsy (tumour bed and normal bladder)

Years one and two only

- *Assessment of bladder capacity (at cystoscopy or by ultra sound or urodynamics)
- *CT Abdomen and pelvis