

# Bladder cancer treatment

## DISCLAIMER:

This website and document is a guide and while it is written by professionals, we advise you to see your doctor if you have any symptoms.

## Treatment options by bladder cancer stage

### Non muscle invasive bladder cancer

If your cancer does not spread into the muscle it is known as non muscle-invasive bladder cancer. The urologist then looks at the pathology report including grade of the cancer, the number of cancer lesions present, size of the lesion and whether the subtype of cancer carcinoma in situ (CIS) is present.

A bladder tumour which is high grade or has invaded into the lamina propria (layer between the bladder lining and muscle) or has carcinoma in situ (CIS) present is considered high risk. If a tumour is low grade but large or recurrent or multiple it may be considered intermediate risk. If a tumour is low grade and small and single it will be low risk.

#### 1. Low risk - non muscle invasive

**Treatment:** *Intravesical (into the bladder) chemotherapy after TURBT*

**Rationale:** This is thought to help prevent floating cancer cells dislodged from the TURBT from seeding and starting new cancer formation.

**Drug name:** Epirubicin or Mitomycin C

#### How is it administered?

After your TURBT procedure you will already have a catheter in place or it will be inserted. A chemotherapy drug will then be inserted with a syringe into the end of the catheter and the catheter will be clamped. This allows a high concentration of the treatment to be applied directly to the areas where cancer cells could remain, potentially destroying these cells and preventing them from re-emerging in the bladder.

The solution is left in the bladder for 1-2 hours, then allowed to drain out through a catheter.



For an overview of bladder cancer treatment options, click **here** to watch a video by Prof Manish Patel.



To understand chemotherapy for non muscle invasive bladder cancer, click **here** to watch a video by Dr Patti Bastick.



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### **What side effects may I experience?**

Because this drug is given directly to the site where it needs to act, side effects are minimised. It may cause localised irritation to the bladder.

### **Symptoms may include**

- Need to urinate frequently and urgently
- Pain with urination

These side effects are short-lived and usually disappear in a couple of days.

## **2. Intermediate risk - non muscle invasive**

### ***Treatment: Intravesical (into the bladder) chemotherapy***

**Duration:** 6 weeks starter regime sometimes followed by a longer maintenance regime.

**Drug name:** Epirubicin or Mitomycin C

## **3. High risk - non muscle invasive**

### ***Treatment - Intravesical immunotherapy (BCG) after TURBT***

**Rationale:** BCG therapy has been shown to delay bladder cancer from becoming more advanced and decreases the need for a cystectomy at a later time.

### **What is BCG?**

BCG is a milder form of the live bacterium that causes tuberculosis.

### **How does BCG work?**

BCG is believed to work by triggering the body's immune system to destroy any cancer cells that remain in the bladder after TURBT.

### **When is BCG given?**

It is given two to three weeks after the last TURBT.

### **How long is BCG given for?**

The treatment is usually given once per week for six weeks (induction) and then less frequently for 1-3 years (maintenance)

### **How is BCG administered?**

BCG is in a liquid solution that is put into the bladder with a catheter. The person then holds the solution in the bladder for two hours before they urinate. During the first hour, your doctor may have you lie for 15 minutes each on your stomach, back, and both sides. When you empty your bladder, you should be sitting down.



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### **What should I do after receiving BCG treatment?**

It is important that you drink extra fluids for several hours after each treatment with BCG so that you will pass more urine. Also, empty your bladder frequently. This will help prevent bladder problems.

### **What are some of the common problems after receiving BCG treatment?**

Some side effects may occur but usually do not need medical attention. These side effects may go away during treatment as your body adjusts to the medicine. Also, your health care professional may be able to tell you about ways to prevent or reduce some of these side effects.

- Frequent urge to urinate
- Increased frequency of urination
- Blood in urine
- Joint pain
- Fever and chills
- Nausea and vomiting
- Painful urination (**severe or continuing**)

After you stop using this medicine, it may still produce some side effects that need attention. Notify your doctor if they are persistent or severe.

### **What is maintenance BCG?**

Maintenance BCG treatment is given for a prolonged period of time to further delay recurrence and progression of the cancer.

It is usually given for at least one year but may be given for up to three years in those at highest risk of recurrence. Maintenance BCG is typically given once per week for three weeks at 3, 6, and 12, 18, 24, 30, 36 months after the initial BCG treatment.

### **Muscle invasive bladder cancer**

Please view these videos to understand the various treatment regimes for muscle-invasive bladder cancer:



**Chemotherapy for muscle invasive bladder cancer**, by Dr Patti Bastick.



**The surgical treatment of bladder cancer**, by Prof David Gillatt.



**Radiation therapy for bladder cancer**, by Dr Patti Bastick.



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## 1. Muscle-invasive non-metastatic bladder cancer

The ideal treatment for this stage of cancer is a radical cystectomy with a urinary diversion. This is the surgical removal of the bladder. When the bladder is surgically removed the urine will need to be drained from the kidneys through a different route. This is usually achieved through the creation of a new bladder.

Patients with the following are suitable for a radical cystectomy:

- Muscle-invasive bladder cancer AND no evidence of metastatic disease
- Superficial bladder cancer and one of the following:
  - Intravesical chemotherapy failed to work
  - Extensive disease not amenable to cystoscopic resection
  - Invasion of the prostate
  - High risk cancer where BCG failed to work
- Rare bladder cancer types: Primary adenocarcinoma, squamous cell cancer, or sarcoma.

Patients with the following are not suitable candidates for a radical cystectomy:

- Extensive bladder cancer disease that has spread into structures surrounding the bladder or beyond.
- Advanced age
- Disorders related to clotting difficulty. (high risk of bleeding in the operation)
- Other medical diseases in which a general anaesthetic or a major operation is very risky:
  - Advanced heart disease
  - Poor lung mechanics

### ***Chemotherapy before surgery (neo-adjuvant chemotherapy)***

#### **What is the benefit of neoadjuvant chemotherapy?**

It helps to eliminate undetectable cancer cells that may be present in other areas of the body in people with invasive bladder cancer. By eliminating these cancer cells, chemotherapy helps to improve survival. Getting chemotherapy prior to surgery also eliminates the possibility that surgical complications will prevent you from being able to get adjuvant ('after surgery') chemotherapy later.

Not everyone is eligible to receive neoadjuvant chemotherapy. Find out from your urologist or oncologist whether you are eligible.

#### **How is neoadjuvant chemotherapy administered?**

Regimens usually include a drug called Cisplatin along with one or more other drugs. The drugs are given intravenously over 3-4 cycles.



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### **What are the side effects of neoadjuvant chemotherapy?**

Chemotherapy works by interfering with the ability of rapidly growing cells (such as cancer cells) to divide or reproduce themselves. Because normal cells in the body are not rapidly growing, they are not affected by chemotherapy. Exceptions to this include cells of the bone marrow (where blood cells are produced), lining of the gastrointestinal tract and hair. These tissues are most affected by chemotherapy, causing the typical side effects (low blood counts, nausea, and hair loss etc).

### **A decision has now been made that you need a radical cystectomy. What's next?**

Making the decision to undergo surgery can be quite daunting. It should always be made in conjunction with a team of experts and your family, friends and support groups. There will be a multidisciplinary medical team (see BEAT's download on your team **here**) working very closely together before, during and after your surgery.

Prior to the surgery you will visit a pre-admission clinic. Here you will be prepared for the operation. This may include some tests, such as:

- Blood tests
- Chest X-ray
- ECG (echocardiogram) to assess your heart

These tests vary depending on what underlying illnesses you may have and will be determined by your surgeon and anaesthetist. The aim is to ensure you that you are fit to undergo a general anaesthetic and lengthy major surgery. Based on your medical history and the test results you may on occasion be reviewed by other specialists such as heart (cardiologist) or lung (pulmonologist) doctors to ensure you are ready for theatre.

If you smoke, the best thing you can do for your health is to quit before surgery. Not only is smoking a risk factor for developing bladder cancer, smoking also increases the risk of developing problems after surgery. Visit <http://www.quitnow.gov.au/> to find out how.

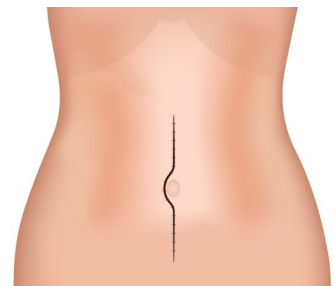
You will also visit the stoma nurse the day before or on the morning of surgery. The stoma nurse will give you some information about living with a stoma which will be reinforced after the surgery. The stoma nurse will also then make some coloured markings on your tummy so the surgeon knows where to place the stoma during the operation.

Some surgeons may alter your diet a few days prior to surgery to a lighter diet switching over to a fluid diet and nothing by mouth the night before surgery. This may also include a laxative or enema to clear the bowel. This is not standard and may vary according to a surgeon's preference.

### **Are there different ways for a cystectomy to be done?**

There are three approaches to a cystectomy. They include:

**1. Open surgery:** The traditional approach is to cut from the navel to pubic bone in the midline. This will result in a scar.



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**2. Laparoscopic surgery:** Keyhole (minimally invasive surgery) is done through small incisions in the abdominal wall. Ports are placed, through which instruments are passed to do the surgery.



**3. Robotic surgery:** Keyhole (minimally invasive surgery) is done through small incisions through in the abdominal wall. Ports are connected to the robotic arms which are controlled by the surgeon.



**What are the benefits or disadvantages of each surgical approach?**

The outcomes in terms of cancer control would be the same for open surgery versus minimally invasive surgery.

Patients undergoing open surgery may experience more pain after surgery and have a longer hospital stay with the converse applicable for minimally invasive surgery.

**What does the cystectomy procedure entail?**

The procedure is performed with the patient under general anaesthetic (you will be asleep and you won't feel, hear or see anything).

The anaesthetist (doctor who puts you to sleep) will administer medications to make you sleep through an intravenous cannula in your arm as well as some gases through the mask applied to your face.

Because it's a major operation you may receive extra lines (drips) for example a central venous line in the neck or a cannula directly into the artery (arterial line). These lines are important for monitoring your heart, lungs and fluid status during the operation. They may remain after your operation especially if you are transferred to the ICU (intensive care unit) after the operation.

**The procedure usually occurs in three parts:**

1. Removal of the bladder and surrounding structures
2. Lymph node dissection
3. Formation of a new bladder



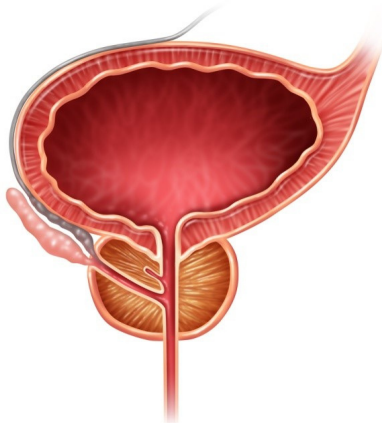
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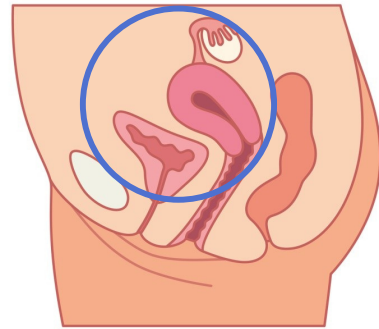
The specimen will then be sent to the laboratory for the pathologist to again assess the stage of your cancer.

### Removal of the bladder and surrounding structures

**For men**, the radical cystectomy includes the removal of the bladder, part of the urethra, lymph nodes, prostate gland and seminal vesicles.



**For women**, the radical cystectomy includes the removal of the bladder, part of the urethra, lymph nodes, ovaries, uterus, cervix, and upper vagina.



### Lymph node dissection

Lymph fluid from the bladder normally drains into lymph nodes (glands) located in the pelvis. If your cancer has spread to these lymph nodes, there is a much higher risk that your cancer has also spread elsewhere. This significantly increases the risk of the cancer recurring at a later time.

An important part of your surgery is to therefore remove all lymph nodes that could contain cancer cells. This includes lymph nodes in the pelvic region, and in some cases, it also includes more distant lymph node groups (which may improve survival).

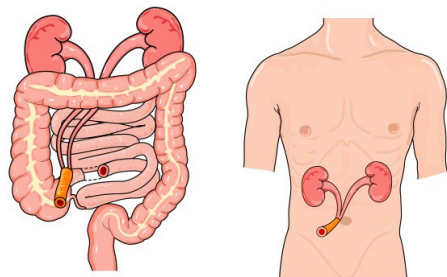
### Formation of a new bladder or urinary diversion

After your bladder is removed, the surgeon must create a new place for urine to be stored. All options include the use of a segment of bowel, which is removed from the small or large intestine.

After removing a segment of bowel, the intestines are reattached so that they function normally. The section of bowel that is removed is cleaned and prepared and then connected to the ureters for urine to drain from the kidneys.

There are three possible options:

**1. Urine can be diverted through a segment of bowel to the skin's surface, where an opening (called a stoma) is created.** A bag is attached to the stoma to collect the urine. This is called an ileal conduit, urostomy or non-continent cutaneous diversion.



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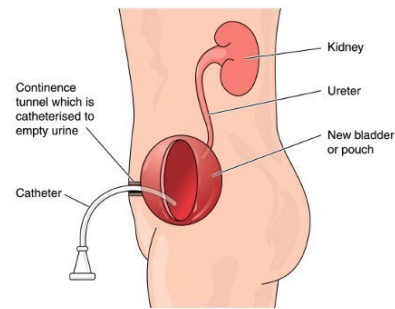
**2. A pouch may be created under the skin of the abdomen using part of the intestine.** Urine collects in the pouch, and you use a catheter to empty the pouch periodically. It is not necessary to wear a bag. This is called a continent cutaneous diversion.



**3. A new bladder may be created from a segment of bowel.** The new bladder is connected to the urethra (the tube through which urine exits the body), allowing the person to urinate normally. **This is called a neobladder.**

The "best" type of urinary diversion depends on you and your surgeon's preference, as well as the extent of your cancer.

After the surgery you may have a stoma (usually on the right side). You may have one or two drain tubes (including one in the urethra).



You will most likely spend one or more days in the ICU after your surgery before being transferred back to the general urology ward, where you will continue to be cared for by your multidisciplinary medical team.

### **What kind of complications may occur during the procedure?**

Anaesthetic related complications are usually rare, but may range from nausea and vomiting to a sore throat.

Surgery related complications may include:

- Bleeding
- Blood clots (lungs [pulmonary embolus] or calves [DVT])
- Heart attack
- Infection
- Pneumonia

### **Chemotherapy after surgery (adjuvant chemotherapy)**

This may be given if more extensive disease is found when the bladder is removed. The following patients may be eligible:

- The tumour extends into the layer of fat surrounding the bladder (stage T3 or higher)
- Cancerous cells are identified in the lymph nodes that were removed during the cystectomy

There is no standard regimen in this situation, but the options are generally the same as in neoadjuvant chemotherapy (see above). You may also consider enrolling in a clinical trial if possible.



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### **Radiation therapy is a curative option for bladder cancer.**

Radiation therapy can be used to cure bladder cancer in selected patients where the cancer has not spread beyond the bladder or the lymph glands in the pelvis.

Radiation therapy may be suitable for patients who:

- Are not fit for surgery due to their other health issues, or
- Are fit and want to attempt to keep their bladder.

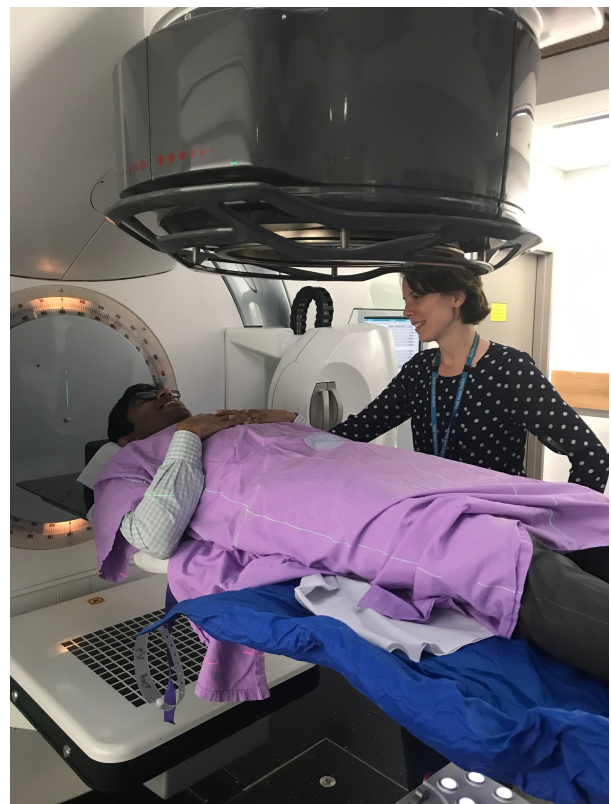
Radiation therapy is often used in combination with medications to make the radiation more effective, including chemotherapy agents or radiosensitising drugs. This approach is called **combined modality bladder sparing treatment or multimodality bladder preservation.**

There are no trials directly comparing surgery to remove the bladder (cystectomy) versus multimodality bladder preservation, however modern studies of bladder preserving treatment report similar overall survival rates to surgery. In general, 70% of people who are treated with multimodality bladder preservation will still have a functional, cancer free bladder at 5 years after treatment, with approximately 1 in 10 patients going on to a cystectomy after radiotherapy.

Ideal candidates for bladder preserving treatment are those who have a small or early stage muscle-invasive cancer, have a bladder that functions well at the start of treatment, and are willing to attend for regular follow up.

### **Radiation Planning**

Radiation therapy is very carefully planned and delivered. The first step is called a “simulation session”, where you will be positioned on a treatment bed with equipment tailored to your body shape to keep you comfortable and help you lie still. You may be asked to empty or fill your bladder prior to getting on the bed. Scans and measurements will be used to design an individualised treatment plan, focusing high energy x-rays to areas containing cancer whilst limiting radiation to surrounding normal tissues. The design process may take 1-2 weeks before treatment commences. You may be asked to have some small, permanent marks left on the skin (tattoos), to help position you on the bed when you return for treatment.

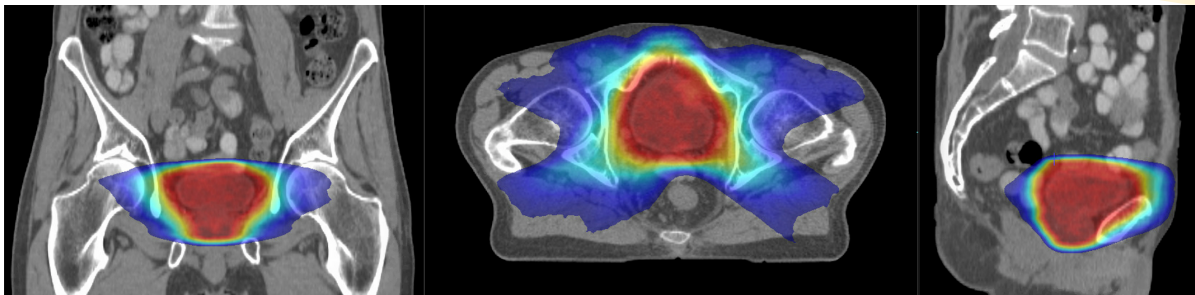


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### Daily treatment

Treatment usually occurs daily, 5 days per week from Monday to Friday, for a total of 4 to 6 weeks. Each treatment session takes about 10-15 minutes. Much of that time is taken up by getting you into the correct position and making sure that you are comfortable, with the treatment itself taking only a few minutes. You will be asked to lie still and the machine will move around you, making some clicking noises when the radiation beam is turned on. You cannot see or feel the radiation being delivered, although occasionally people describe a warm feeling in the area being treated. After each session is finished, there is no radiation left in the body and you are free to be around other people. Patients are often able to drive themselves to and from treatment, and some patients will continue to work during treatment.



### Side effects

Side effects from radiation therapy vary from patient to patient. “Short term” side effects typically develop in the second half of treatment, peak 1-2 weeks after treatment finishes, then gradually improve 6-8 weeks after treatment finishes.

Common **short term side effects** during radiation therapy to the bladder include:

- Feeling tired
- Needing to pass urine more frequently and “urgently” i.e. not getting the same amount of warning when you need to urinate
- Burning/stinging when you pass urine
- Loose bowel motions or discomfort passing faeces
- Abdominal discomfort/bloating
- In women, vaginal dryness and irritation
- Minor skin redness/irritation
- Loss of some pubic hair

Most short term side effects resolve within 3 months of treatment, but some patients experience persistent side effects after radiation therapy or side effects that occur months or years later. These are called “long term” or “late” side effects, and may be permanent. In general, 70% of patients experience no long term side effects from radiation therapy, 10-20% experience mild ongoing symptoms not requiring treatment, and 1-10% experience ongoing symptoms requiring further investigation or treatment.



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Potential **long term side effects** of radiation therapy to the bladder include:

- Needing to pass urine more frequently or urgently
- Needing to open your bowels more frequently or urgently
- Bleeding from the back passage when you open your bowels
- Swelling of the legs (this type of swelling is called lymphoedema and only occurs in some patients who have had the lymph glands treated as well as the bladder)
- In men, difficulty getting or maintaining an erection, and reduced sperm count
- In women, premature menopause, and vaginal dryness and/or narrowing that can impact on normal sexual function

### **Uncommon long term side effects**

- Urinary incontinence or urine leakage that requires you to wear a pad
- A bladder that has significantly reduced capacity such that you would prefer to have your bladder removed
- Development of a second cancer (rare)

### **Things you can do to reduce the risk of side effects**

#### **1. Dietary advice**

- Eat a well balanced diet during and after radiation therapy
- If troubled by diarrhea, you may be advised to follow a low fibre diet and may be given additional medications to reduce the number of bowel motions
- Consultation with a dietitian is sometimes recommended

#### **2. Skin care**

- Apply a basic moisturiser such as sorbolene cream to the treated area regularly during radiation therapy
- Wear loose and comfortable clothing during radiation therapy
- Avoid exposing skin in the treatment area to heat lamps or direct sunlight during radiation therapy

#### **4. Stopping smoking**

- Continuing to smoke reduces the chances of radiation therapy being successful
- Smoking also significantly increases the risk of serious late side effects developing
- Stopping smoking also reduces the risk of a second cancer developing in the future

#### **5. Vaginal dilator use (in women)**

- The risk of vaginal shortening and narrowing can be reduced by regular stretching of the vagina following completion of treatment. This can be achieved by the self-application of vaginal dilators, which your radiation oncologist will educate you about if applicable.



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### **Follow up**

You will be reviewed by your radiation oncologist at regular intervals to assess and manage any side effects of radiation therapy. Follow up cystoscopy (where your urologist inserts a thin flexible camera into the bladder) will also be performed regularly to check that the cancer has responded to radiation therapy and to monitor for signs the cancer recurring. The first cystoscopy is normally at about 12 weeks after radiation has finished. These regular appointments to look in the bladder after treatment are important, as if the cancer recurs or a new bladder cancer develops and it is picked up at an early stage, the cancer can still be cured by having an operation to remove the bladder (cystectomy).

## **2. Muscle-invasive metastatic bladder cancer**

Patients with bladder cancer that has spread outside the bladder won't be candidates for surgery but will be eligible for one or more of the following treatments:

- Chemotherapy
- Immunotherapy
- Radiation therapy

### **Chemotherapy**

The common chemotherapy drugs used are Cisplatin and Gemcitabine. They work by interfering with the ability of rapidly growing cells (such as cancer cells) to divide or reproduce themselves. They are administered intravenously through a cannula in your arm as an outpatient, and given as a cycle over a period of weeks.

### **What are common side effects?**

Because normal cells in the body are not rapidly growing, they are not affected by chemotherapy. Exceptions to this include cells of the bone marrow (where blood cells are produced), lining of the gastrointestinal tract and hair. These tissues are affected most by chemotherapy, causing the typical side effects (low blood counts, nausea, and hair loss etc).

### **Immunotherapy**

Immunotherapy is usually reserved for patients whose cancers don't respond to chemotherapy or in people who can't tolerate or are ineligible for chemotherapy.

Some commonly used immunotherapy drugs are Pembrolizumab and Atezolizumab. These drugs work by triggering the body's immune system to systemically destroy cancer cells. They are administered intravenously through a cannula in your arm as an outpatient.

### **What are common side effects?**

Because immunotherapy works in a positive way within the body, it has fewer side effects compared to chemotherapy and is generally better tolerated. Side effects may include:

- Feeling tired (fatigue)
- Diarrhoea
- Fever
- Nausea and vomiting



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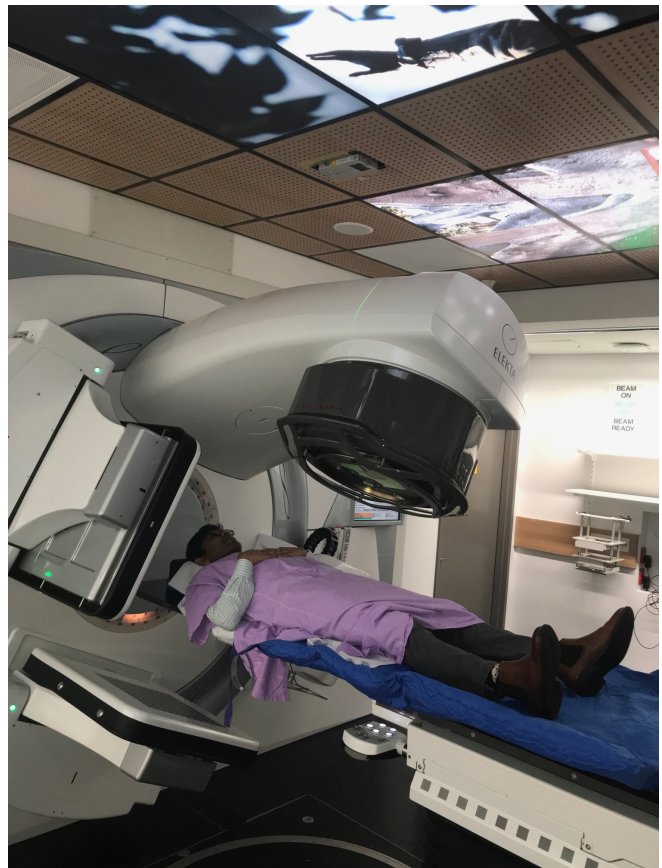
## Radiation therapy

Radiation therapy is often used for patients when the cancer in the bladder is advanced or when the cancer has spread from the bladder to other areas in the body. Your radiation oncologist will assess whether this treatment is suitable for you and explain what is involved.

Radiation therapy can be used to shrink the cancer in the bladder, stop bleeding in the bladder and to help with pain that the cancer may be causing. It can also be directed at other body sites, for symptoms such as pain from cancer which has spread to the bones.

Radiation therapy is very carefully planned and delivered. The first step is called a “simulation session”, where you will be positioned on a treatment bed with equipment tailored to your body shape to keep you comfortable and help you lie still. Scans and measurements will be used to design an individualised treatment plan, focusing high energy x-rays to cancer cells in the problem area, whilst limiting radiation to surrounding normal tissues. The design process may take a few days before treatment commences. You may be asked to have some small, permanent marks left on the skin (tattoos), to help position you on the bed when you return for treatment.

The number of treatments that you need can range from as little as a single treatment to a few weeks of daily treatment. Your doctor will explain how many treatments that you need. Each treatment session takes about 10-15 minutes. Much of that time is taken up by getting you into the correct position and making sure that you are comfortable, with the treatment itself taking only a few minutes. You will be asked to lie still and the machine will move around you, making some clicking noises when the radiation beam is turned on. You cannot see or feel the radiation being delivered, although occasionally people describe a warm feeling in the area being treated. After each session is finished, there is no radiation left in the body and you are free to be around other people.



The potential side effects will depend on which part of the body is being treated, but are usually mild. Your radiation oncology doctor and nursing team will help you manage these symptoms if they occur.



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## Clinical trials

If you don't respond to standard chemotherapy or even immunotherapy then you may be eligible to take part in a clinical trial.

Other than the benefits in advancing medical science, being part of a clinical trial often involves dedicated care and support by the clinical trial team.

To find out more about clinical trials speak to your oncologist or visit: <https://www.australianclinicaltrials.gov.au/>

If there is a trial that you might have heard about taking place overseas find out all the facts and discuss it with your oncologist in Australia first before getting involved.



To learn more about Clinical Trials, click **here** to watch a video by Dr Patti Bastick.

## Treatment of rare bladder cancers

These are bladder cancers that are not urothelial (transitional cell) cancer. Combined they make up only 5% of all bladder cancers. They include:

- Squamous cell carcinoma
- Adenocarcinoma
- Small cell carcinoma
- Sarcoma
- Plasmacytoid
- Micropapillary variant

Many of these cancers don't respond to conventional intravesical chemotherapy or immunotherapy. In most cases the first line of treatment is a radical cystectomy, in some cases, followed by chemotherapy, immunotherapy and/or radiation. For some of the adenocarcinomas it may be possible to only take out part of the bladder known as a partial cystectomy.

Your urologist and oncologist will work with you to agree the most appropriate course of action if you are suffering from a rare (non-urothelial) cancer.

## Alternative therapies

There are many alternative therapies available, however there is not enough scientific evidence to support their efficacy in preventing or curing bladder cancer. Always discuss alternative therapies with your oncologist before use.



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