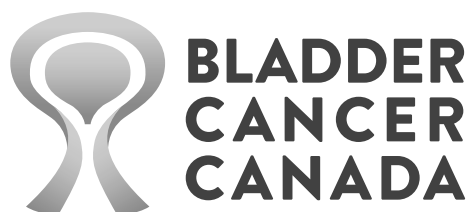


BLADDER CANCER PATIENT GUIDEBOOK

FOR PATIENTS WITH METASTATIC
BLADDER CANCER



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YOU ARE NOT ALONE



This Patient Guidebook was created by people just like you – bladder cancer patients and their caregivers. It's designed to offer you support, encouragement and tips on how to deal with the procedures and treatments for your bladder cancer. It can help you understand your disease and what to expect, the treatments you may be offered and how to manage your disease and its side effects.

We're not medical professionals and you should always turn to your medical team for advice first. But we have been where you are now and have experienced what you are feeling. To ensure accuracy, this Guidebook has been reviewed by a team of medical professionals.

This Guidebook will talk about common approaches to treating metastatic bladder cancer. Keep in mind that there can be some differences, depending on the practices of your medical team and on your specific situation. We'll not be using a lot of medical language, except where it might help you better communicate with your medical team and understand your disease. You'll find a handy glossary of terms on Bladder Cancer Canada's website at <https://bladdercancerCanada.org>.

Remember, you're not alone. All of us at Bladder Cancer Canada are passionate about helping you to live a full and satisfying life – even after a diagnosis of bladder cancer. We're doing it and so can you.

WHAT CAUSES BLADDER CANCER?

As with many types of cancer, one of the leading risk factors of the disease is smoking. Those who smoke may be up to four times more likely to get bladder cancer. People who work with certain chemicals may also be at risk – leather workers, hairdressers, mechanics and painters, among other occupations. Exposure to radiation and certain chemotherapy (such as cyclophosphamide) has also been linked to bladder cancer. Caucasian men may also be at greater risk.

But the simple truth is that many will develop bladder cancer for no known reason. You may be one of those people. At this point, asking “why” is not nearly as helpful as focusing on “what now.” Many of us never knew bladder cancer existed before our diagnosis. But, it's more common than you might think, as it's the 5th most common cancer in Canada.

WHAT IS METASTATIC BLADDER CANCER?

Bladder cancer is considered “metastatic” when the cancer has spread from the bladder to other parts of the body such as the lymph nodes, liver, lungs and bone. It’s also called advanced stage IV bladder cancer. Approximately 10-15% of patients are diagnosed at this stage.

Metastatic bladder cancer can be called “de novo,” which means that bladder cancer has already metastasized when it’s first diagnosed. Alternatively, it could metastasize after initial therapy for cancer that has not spread beyond the bladder.

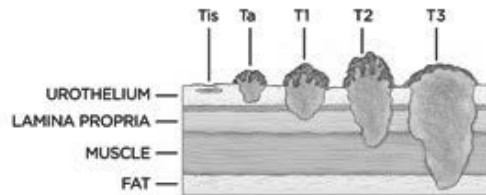
Metastatic disease is associated with a more limited life expectancy than cancer that is diagnosed at an earlier stage. Treatment is geared toward prolonging survival, shrinking or slowing growth of the tumour, easing symptoms and improving quality of life. In other words, helping you live as well as you can for as long as you can. In rare cases, treatment of metastatic bladder cancer may result in a cure.

This Guidebook will help you better understand how metastatic bladder cancer is treated, what side-effects you might experience and how your cancer journey can be managed.

Although we do not specifically deal with upper urinary tract cancer, much of this Guidebook can also apply to cancers of the renal pelvis (where urine collects in the kidneys before it travels to the ureters and bladder), renal calyces (spaces deep in the kidneys), and the ureters (thin tubes, made of muscle, which move urine from the kidney to the bladder).

STAGING AND GRADING YOUR BLADDER CANCER

Laboratory analysis of the material taken out during the Transurethral Resection of Bladder Tumour (TURBT) is used to determine the type and stage of the cancer. A TURBT is a surgical procedure done through the urethra under general or regional anesthesia, to biopsy any abnormal tissue that is found during a cystoscopy. Staging classifies a cancer based on its extent in the body.



STAGING

Staging includes a Tumour category (T) that describes the tumour itself:

T0 - Cancer has only grown into the centre of your bladder. It hasn’t spread into the tissues or muscle of your bladder wall itself. It hasn’t spread to your lymph nodes or other organs, either.

Tis - Carcinoma in situ (flat tumour), sometimes called Cis.

Ta - Non-invasive papillary carcinoma.

T1 - The tumour is in the first layer of the bladder lining, but not the surrounding muscle.

T2 - The tumour has grown into the muscle. In stage T2a, the tumour is in the inner half of the muscle layer and in stage T2b, the outer half.

T3 - The tumour has spread to the fatty layer around the bladder muscle. If this spread is only seen under the microscope, the tumour is T3a, but if it is seen on scans or felt on examination it is T3b.

T4 - The tumour has spread to adjacent organs outside the bladder (T4a) such as the bowel, prostate, vagina or fixed to the pelvis (T4b).

In addition, the Node (N) category describes whether or not the bladder cancer has spread to lymph nodes near the bladder. If it has, then the N category describes exactly which lymph nodes the cancer has affected. The N staging category includes: NX, N0, N1, N2, and N3.

The Metastasis (M) category describes whether the cancer has spread to organs and/or lymph nodes in other parts of the body that are more distant from the bladder. The category M1 means that the cancer has spread to distant parts of the body and the category M0 means that the cancer has not spread to distant parts of the body.

Bear in mind that it can be somewhat difficult for your medical team to know the true extent of your tumour without surgery. That’s because there may be a difference between “clinical staging” and “pathological staging.”

The TURBT is part of the “clinical staging” process, which is done before treatment. Clinical staging also includes a physical exam, imaging tests (such as a CAT scan), laboratory tests (such as blood tests), and biopsies (such as those done following the TURBT). Pathological staging is determined by laboratory analysis after surgical removal of the bladder (cystectomy).

Complete staging combines the results of the clinical staging with the surgical results. Sometimes a biopsy may be taken from another part of your body to determine if an abnormality seen on a scan is from bladder cancer, another type of cancer, or something else entirely.

GRADING

In addition to showing what stage your cancer is, the pathology report following your TURBT will also generally show whether your tumour is “high grade” or “low grade.”

IMPORTANT

Keep a copy of the pathology report, which will tell you the grade and stage of your tumour (how deep it is through in the bladder) but not where else the cancer is or may be.

SIGNS AND SYMPTOMS OF METASTATIC BLADDER CANCER

Many signs and symptoms of metastatic bladder are similar to those of all types of bladder cancer:

- Blood or blood clots in the urine
- Pain or burning sensation when urinating
- Frequent urination, especially at night
- The urge to urinate, even though the bladder is empty
- Lower back pain on one side

In addition, metastatic bladder cancer may include:

- Weight loss and loss of appetite
- Fatigue, weakness and general discomfort
- Swelling in the feet
- Bone pain
- Swollen lymph nodes
- Shortness of breath or coughing

It’s important to note that you may not have all these signs and symptoms. Also, some of the symptoms listed above may be signs of other conditions. The symptoms are also dependent on which part of the body the cancer has spread to. Consult your health care provider if you are concerned about any of these symptoms.

HOW IS METASTATIC BLADDER CANCER TREATED?

Urothelial cancer (also called transitional cell carcinoma) is the most common type of bladder cancer. The standard initial (or first-line) treatment for metastatic urothelial cancer is chemotherapy, using a combination of anti-cancer drugs based on Cisplatin, the most common drug used in the treatment of metastatic bladder cancer.

Cisplatin is a platinum-based drug that kills cancer cells by damaging their DNA and stopping them from dividing. Depending on the dosage, Cisplatin can affect the nerves, inner ear and kidneys.

You’re eligible for this type of chemotherapy if you’re medically fit. Being considered medically fit involves assessment of various factors, including:

- Kidney function
- Heart function
- Performance status (a score that estimates your ability to perform certain activities of daily living without the help of others)
- Hearing capacity
- Existing peripheral neuropathy (peripheral neuropathy is a type of nerve damage that usually causes pain, numbness or tingling in the fingers and toes, but can progress up the limbs to involve the feet and legs, hands and arms)
- Other factors your medical team may consider important

Fifty percent of people with advanced urothelial cancer are not eligible for Cisplatin-based chemotherapy, so alternative treatment options are considered.

These can include combinations using Carboplatin, or nonplatinum-based drugs, such as gemcitabine, docetaxel or paclitaxel. In patients who are not eligible for Cisplatin, immunotherapy may be beneficial, but this requires further study and is not yet approved in this setting in Canada.

See the section on immunotherapy on page 5 for more details.

SIDE EFFECTS OF CHEMOTHERAPY

Some common side effects of chemotherapy include fatigue; increased risk of infection and bleeding; hearing problems; bowel changes; decreased kidney function; peripheral nerve damage, tingling and numbness (neuropathy), hair thinning or loss; skin rash; weight changes; anemia (low red blood cell counts); and thrombocytopenia (low platelets resulting in risk of bleeding).

There is also a small risk of developing clots in the blood vessels. Nausea and vomiting can occur with chemotherapy, however there are very good supportive medications to help with this and these symptoms are usually very well controlled.

Your cancer care team will review these side effects prior to starting chemotherapy. You should contact your cancer care team if you're experiencing these side effects. However, you should seek immediate help for urgent concerns including having a fever (ask your medical team how they define "fever" in this situation), signs and symptoms of an allergic reaction, unresolved nausea, vomiting and diarrhea and any signs of bleeding.

WHEN INITIAL TREATMENT DOESN'T WORK

Although many patients will respond to the initial treatments we've been discussing, it doesn't work in all patients. In some patients, the disease may eventually progress after initial therapy and secondary ("second-line" or additional) therapy could then be offered.

Immunotherapy as a secondary treatment might be offered to you if the disease has progressed, in spite of receiving platinum-based chemotherapy. (See section on immunotherapy for more details.)

Secondary chemotherapy would be offered to you if you are not a candidate for immunotherapy or for those of you whose bladder cancer progresses during or after immunotherapy. No single second-line chemotherapy treatment plan is considered to be the standard secondary therapy, so your oncologist will discuss plans with you.

IMMUNOTHERAPY FOR BLADDER CANCER

Immunotherapy stimulates the body's defenses to attack and kill cancer cells. There are two types of immunotherapy used to treat bladder cancer:

1. Cancer Vaccines – Bacillus Calmette–Guérin (BCG) vaccine is given intravesically (into the bladder via the urethra) to treat nonmuscle-invasive (superficial) bladder cancer. It is a live bacterium that attracts immune cells, which then attack cancer cells.

2. Immune Checkpoint Inhibitors – This type of immunotherapy works by stimulating the immune system, allowing immune cells to attack cancer cells. Immune checkpoint inhibitors are types of drugs that block certain proteins on the surface of some types of immune cells, such as T cells, and some cancer cells.

These proteins help keep immune responses in check and can keep T cells from killing cancer cells. When these proteins are blocked, the "brakes" on the immune system are released and T cells are able to kill cancer cells better.

These drugs are given intravenously, typically every two to four weeks. Research into and clinical trials of immunotherapy drugs and approvals for their use in Canada is ongoing.

Please discuss with your oncologist which immunotherapy drugs are currently available and which ones your oncologist uses. Your health care team will consider your personal needs to plan the drugs, doses and schedules of immunotherapy.

Side effects of Immunotherapy

Side effects of these drugs can include fatigue, loss of appetite, an allergic reaction, skin rashes and itchy skin. Since these medications work by removing the "brakes" on the body's immune system, they can also cause inflammation of any normal tissue in the body. This is because the immune system can start attacking other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands or other organs.

It's very important to promptly report any new side effects to your health care team, both during or after treatment with immune checkpoint inhibitors. If serious side effects do occur, treatment may need to be held or stopped and you may be provided with high doses of corticosteroids (man-made drugs that closely resemble cortisol, a hormone that your adrenal glands produce naturally) to suppress your immune system.

Prompt recognition and treatment of these side effects may lessen the severity and duration overall, so it's important to report any new or unusual side effects to your health care team as soon as possible.

Immunotherapy may not be recommended for all patients. Immunotherapy may also be used in combination with other treatments, such as surgery, radiation or chemotherapy. This use is currently limited to clinical trials.

RADIOTHERAPY

Radiotherapy can be offered to manage your metastatic bladder cancer. This can be offered for a variety of reasons, including alleviating pain when the cancer has spread to the bones (bone metastases) and reduction in urinary symptoms or bleeding.

Treatment of Bone Metastases

You may be offered bisphosphonates if you have bone metastases. Bisphosphonates are a type (or class) of drugs that prevent the loss of bone density and play an important role in management of bone metastases.

This treatment reduces skeletal-related events (such as fractures and spinal cord compression), manages increased calcium levels in the body, and also manages pain related to bone metastases.

IMPORTANT

Diagnosis of metastatic bladder cancer can be challenging. It's vital that you ask for support and maintain a healthy lifestyle.

Regular exercise is important and recommended at every stage of your treatment. It reduces cancer and treatment-related fatigue and improves quality of life.

To manage side effects from treatment it's also essential that you eat well during your treatment. Try to limit alcoholic drinks, red meat, processed foods and increase your intake of plant-based foods including fruits, vegetables and legumes.

If you experience treatment-related side effects, such as poor appetite, taste changes, dry mouth, difficulty chewing or swallowing, consult your health care provider and registered dietitian at your cancer care centre for advice.

Certain substances in foods and medications can interfere with chemotherapy or immunotherapy. Talk to your oncologist or pharmacist before starting your chemotherapy and immunotherapy. Do not start a new medication or supplement prior to consulting your oncologist while you are on these treatments.

Immunotherapy and Clinical Trials

As immunotherapy for the treatment of bladder cancer is relatively new, some treatments may be approved by Health Canada, but may not yet be covered by your provincial or private drug program. Others may only be available through a clinical trial or a patient access program.

A clinical trial is a research study that tests how well a new medical approach works in people with a certain disease. Each study answers scientific questions and tries to find better ways to prevent, screen for, diagnose, or treat a disease such as bladder cancer.

By participating in a clinical trial, you'll be helping researchers answer important questions that will further the development of new effective treatments. Clinical trials may also provide you with another option in your treatment plan that might not be available to you otherwise. Participation in a clinical trial is voluntary and you may withdraw from them at any time.

Clinical trial websites will help you find clinical trials that may be available in your area. Here's one website you can check: www.canadiancancertrials.ca. This site lists Canadian trials only. You can narrow your search by selecting bladder cancer under "Select a Cancer Type." You may need to select "Show More," if bladder cancer does not display on the list you see. You can also search by province, city or trial centre.

You can also go to clinicaltrials.gov to see what is going on in North America.

It's very important that you discuss with your medical team whether a clinical trial is right for you. Talk to your doctor about the options and the right treatment program for you.

PALLIATIVE CARE

Palliative Care involves symptom control as well as social, spiritual and psychological support. It's provided by a specially-trained team of doctors, nurses and other professionals, such as nutritionists or social workers, who work together to provide support. Palliative care improves quality of life and is an integral part of metastatic bladder cancer management. You'll be provided supportive and palliative care throughout your cancer journey.

This type of care treats pain, depression, shortness of breath, fatigue, constipation, nausea, loss of appetite, difficulty sleeping, anxiety and any other symptoms that may be causing you distress.

Palliative care can be provided along with curative treatment and may even begin at the time of diagnosis. It can be provided by your regular doctors and health care team or a specific palliative care team.

The Value of a Palliative Care Team Referral

Because palliative care teams specialize in dealing with the full range of cancer symptoms, they can ensure that you enjoy the best quality of life possible. They'll help you sort out your immediate concerns, like worrying about

how chemotherapy or radiation might make you feel, or what impact surgery may have, or if you'll lose your hair, or what will happen if you end treatment. Palliative care team members will help you with the bigger-picture things, like deciding what it is you value most in life or weighing the effects of a given treatment against those of the disease itself. It is important to remember that palliative care does not necessarily mean end of life care or no active treatment; it can complement active cancer treatment to make the experience easier.

Don't hesitate to call Bladder Cancer Canada and ask to speak with someone who has gone through the diagnosis and treatment of metastatic bladder cancer. We have peer support volunteers who will answer any questions you have, based on their own experience and acquired knowledge. It's a big help to chat with someone who has been in your shoes – and is surviving and thriving. We know. We have been there!

WHAT CAN I DO?

Established in 2009 by two bladder cancer survivors, Bladder Cancer Canada was the first Canadian patient advocacy organization dedicated to bladder cancer issues. BCC is a national registered charity and the only one devoted to bladder cancer patients and survivors and the caregivers who support them. BCC does not receive any government funding and relies on donations to offer programs and services, such as this free Guidebook, to patients and their families.

Support us

Individual donations are greatly appreciated, and tax receipts are issued for donations of \$20 or more. Donations can be made online at www.bladdercancer canada.org or by calling 1-866-674-8889. Your support will help BCC to continue and expand our programs and services to help even more patients and caregivers like you.

Thank you.

Walk with us

Each September, Bladder Cancer Canada holds awareness walks in numerous cities across Canada. The walks are one of the main sources of funding for

Bladder Cancer Canada and raise approximately two-thirds of our funds for the entire year for patient support programs, awareness initiatives, and bladder cancer research. A walk in the park is not a cure, but it's a good start. Join us at **BCCwalk.ca**

Spread the word

Tell your friends, family and healthcare providers about bladder cancer and Bladder Cancer Canada. You can speak with others on the same journey and be an encouragement and a lifeline to them. To find out how you can help—or to get help yourself—go to the Bladder Cancer Canada website at www.bladdercancer canada.org. Our website has excellent, reliable, and active discussion forums where you can ask questions or share your story. You can also sign up for our e-newsletter to stay up-to-date on upcoming events and research news.

We wish you every success in your journey with bladder cancer.

Let us know how we can help you. That's why we are here!



HELPFUL WEBSITES

- **Bladder Cancer Canada**
<https://www.bladdercancer canada.org>
- **Bladder Cancer Advocacy Network (BCAN US)**
<http://www.bcan.org/>
- **Canadian Cancer Society**
<http://www.cancer.ca/en/cancer-information/cancer-type/bladder/bladder-cancer/?region=on>
- **Canadian Urological Association**
<http://www.cua.org/>
- **Cleveland Clinic**
<https://my.clevelandclinic.org/health/diseases/14326-bladder-cancer>
- **Cornell Urology**
<http://urology.weillcornell.org/bladder-cancer>
- **Johns Hopkins**
<http://urology.jhu.edu/bladder/>
- **Mayo Clinic**
<https://www.mayoclinic.org/diseases-conditions/bladder-cancer/symptoms-causes/syc-20356104>
- **National Cancer Institute (US)**
<http://www.cancer.gov/cancertopics/types/bladder>

ABOUT BLADDER CANCER CANADA (BCC)

We are a national charity with a mission to:

- Help bladder cancer patients and their support teams address the day-to-day issues of this disease
- Increase awareness of bladder cancer among the general public and medical community
- Fund research which pursues the diagnosis, treatment and elimination of bladder cancer.

Bladder cancer awareness among Canadians at a relatively early stage. There is little public awareness of the symptoms of the disease and, unless diagnosed with this cancer, most people are not well educated about it.

Bladder Cancer Canada is working to change this.

For more information, visit our website at www.bladdercancerCanada.org.

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SPECIAL THANK YOU NOTES

We extend special appreciation to the medical review panel for this Guidebook, who provided invaluable feedback and ensured accuracy:

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