



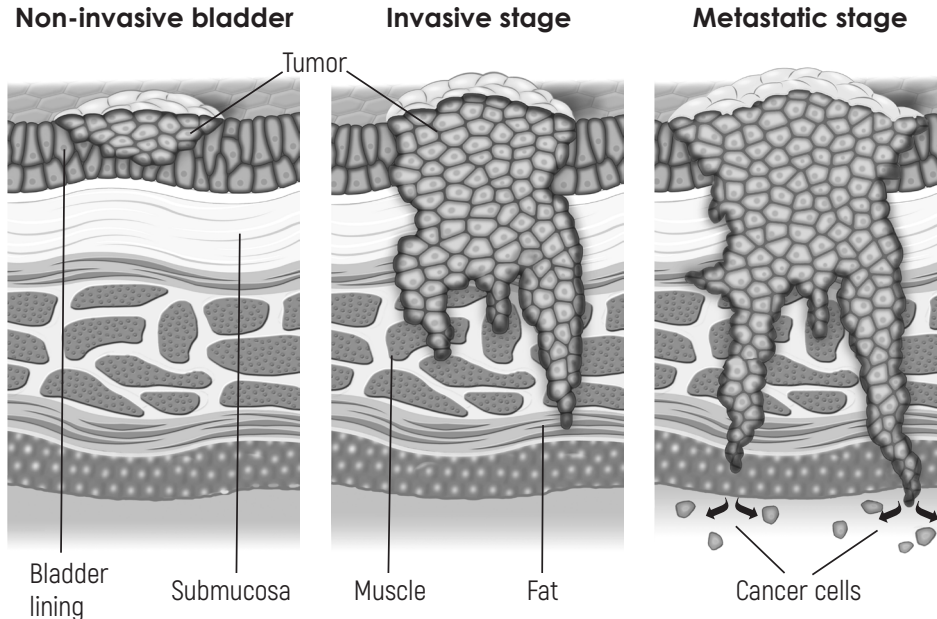
Patient Guide to Metastatic Urothelial Carcinoma Treatment

What is metastatic urothelial carcinoma?

Urothelial carcinoma is the most common type of bladder cancer. It is called that because it starts in the cells that line the inside of the bladder, which are called urothelial cells. Urothelial carcinomas can affect the bladder as well as the upper urinary tract (including the ureters which are the tubes that carry urine from the kidneys to the bladder).

Bladder cancers are often divided into groups based on how far they have spread:

- Non-invasive bladder cancer only affects the inner lining of the bladder.
- Non-invasive bladder cancer may also describe cancer that has grown past the inner lining but has not grown into the muscular layer of the bladder. (This is also known as non-muscle-invasive bladder cancer).
- Muscle-invasive bladder cancer has grown into the muscles deep within the bladder wall and sometimes into the fat that surrounds the bladder.
- Metastatic bladder cancer has spread to other parts of the body, such as the lungs, liver or bone. Metastatic cancer is often described as "unresectable," meaning that it cannot be surgically removed or "resected."



So, metastatic urothelial carcinoma (MUC) is a type of bladder cancer that has spread to other parts of the body.

What is cancer staging?

Staging is a way to classify a cancer based on where it is first diagnosed and how far it has spread. This helps your doctor choose the right treatment for you.

Bladder cancer is usually staged using the TNM system, which classifies cancers into five stages, from 0 to 4. The higher the stage number, the more the cancer has spread (table 1).

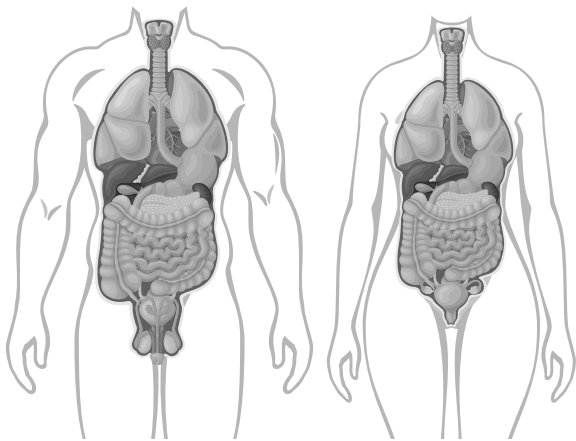
Table 1: The characteristics defining the stages of urothelial cancer

| Stage | Urothelial Cancer Classification |
|-------|--|
| 0 | Cancerous cells are found on or near the surface of the bladder |
| I | Cancerous cells are found in the connective tissue lining the bladder |
| II | Cancerous cells have spread to the muscle wall lining the bladder |
| III | Cancer cells have spread to the fatty layer of tissue that surrounds the bladder |
| IV | Cancerous cells have spread to structures beyond the bladder |

In the TNM system, stage IVA is when the cancer has grown into the pelvic wall or the abdominal wall (locally advanced) or has spread to lymph nodes distant from the bladder. Stage IVB is metastatic cancer, which has spread to other parts of the body.

Where has my cancer spread to?

Ask your doctor to mark the places your cancer has spread on this diagram:



How is metastatic urothelial carcinoma treated?

Chemotherapy (drugs that kill cancer cells) is usually the first treatment offered in MUC. It is used to improve survival and quality of life.

Some patients receive **immunotherapy** (a treatment that increases your own immune system's ability to detect and fight cancer) after the chemotherapy is finished.

Targeted therapy (drugs that target specific molecules on or inside cancer cells) is used in some patients who have cancers with specific genetic changes. It is used after chemotherapy.

Antibody-drug conjugates are a new kind of treatment that combine an antibody that finds proteins made by cancer cells with a drug that destroys those cancer cells.

You may also be offered **radiation therapy** (also called **radiotherapy**). This can have a variety of uses, including reducing bone pain if your cancer has spread to your bones, and reducing urinary symptoms or bleeding. Radiation therapy is only given to the bladder or the site where the cancer has spread to and is used to help minimize symptoms caused by the cancer.

Surgery is sometimes (though rarely) used in patients with MUC. It is most often used to help control symptoms such as bleeding or pain.

If a clinical trial is available for patients with MUC, you may choose to join it. Clinical trials are studies to determine whether a new drug (or drugs) is better than the currently used drugs. If you join one, you won't always know whether you are getting the new drug or the currently used drugs, but you will receive excellent treatment either way.

What chemotherapy drugs are there?

The first choice of chemotherapy drug is usually cisplatin. You're eligible for cisplatin treatment if you're medically fit. Finding out whether you are medically fit involves your doctor assessing certain factors about you including:

- Performance status (how well you perform activities of daily living)
- Kidney function
- Hearing capacity
- Peripheral neuropathy (nerve damage that usually affects hands, feet, arms and legs)
- Heart function

If cisplatin can't be used, carboplatin is usually used instead. Most people who can't take cisplatin can take carboplatin.

If you receive cisplatin or carboplatin, it will probably be combined with other chemotherapy drugs to make it more effective. A drug called gemcitabine is most commonly used with either cisplatin or carboplatin, but you may receive other drugs such as docetaxel or paclitaxel.

What immunotherapy drugs are there?

The immunotherapy drugs most often recommended for MUC treatment are called immune checkpoint inhibitors. They include pembrolizumab, durvalumab, atezolizumab and avelumab.

What is maintenance therapy?

Maintenance therapy is treatment that is given to patients whose cancer hasn't progressed after chemotherapy (got better or didn't get worse). Its purpose is to provide a different type of treatment to cancer cells that were not destroyed by the initial chemotherapy.

In Canada, an immune checkpoint inhibitor called avelumab can be used as maintenance therapy after cisplatin or carboplatin chemotherapy in patients whose cancer didn't progress with chemotherapy.

How long will my treatment last?

It depends on the kind of treatment you are receiving. Chemotherapy is usually done for four to six "cycles" where a cycle takes three or four weeks. You will only be given chemotherapy on one to two days per cycle.

Immunotherapy is given as one dose every two to four weeks and can be continued as long as your cancer isn't getting worse and you aren't having troublesome side effects.

Maintenance therapy with the specific agent called avelumab is given once every two weeks and can also be continued as long as your cancer isn't getting worse and you aren't having troublesome side effects.

Targeted therapy with an approved drug named erdafitinib is given every day as tablets to take orally. It is also continued as long as your cancer isn't getting worse and you aren't having troublesome side effects. It is only useful if your cancer is found to have a mutation in a gene called "fibroblast growth factor receptor or FGFR". This mutation is found in approximately 10-15% of all metastatic urothelial cancers. More research is being done to better understand the role of FGFR.

The antibody-drug conjugate approved in Canada is called enfortumab-vedotin and is given on three days of a four-week cycle, and is also continued as long as your cancer isn't getting worse and you aren't having troublesome side effects.

What about side effects?

Every medication causes side effects, some worse than others. Your doctor and other members of your healthcare team will work with you to help manage these side effects. You deserve a reasonable quality of life during your treatments and your healthcare team members will help you achieve that.

Can my treatment be modified to suit me better?

If you have unmanageable side effects, your doctor will change your treatment or your dose to help manage those side effects. Over the weeks or months that your treatment is given, your doctor will also review how well it is working and make changes if it isn't working well enough. You will have regular follow-up visits and your doctor will monitor your symptoms and your cancer, usually with imaging (such as computed tomography or CT scans).

Where will I receive my treatments?

Most of the time, your treatment plan will be worked out in a cancer centre, which is generally a large hospital in a major city. You may have to travel to the cancer centre to get your treatments. However, in some parts of Canada, smaller centres—such as infusion centres and local hospitals—can provide your treatments. Ask your doctor about getting treatment closer to home if that better suits your needs.

Who will be part of my healthcare team?

Every hospital is a little bit different, but your healthcare team will usually include your family doctor, your oncologist, one or more nurses or nurse practitioners, and your pharmacist. You may also work with an educator, a social worker, a psychologist, a physiotherapist, a sexologist, a stoma therapist, a radiologist, a radiation oncologist, a surgeon, a urologist or a pain specialist. All these individuals have the goal of helping and supporting you.

What else should I know before starting treatment?

Learning that you have cancer can be overwhelming, and it's normal to have a lot of questions. There are many possible treatment options with the goal of prolonging your life as well as maintaining your quality of life. Although MUC is not usually curable, treatments can often provide sustained benefits and can help to manage your cancer. Talk to your healthcare team to learn more about what is best suited for you.

It's important to ask for support and maintain a healthy lifestyle during your treatment:

- Regular exercise is helpful at all stages of treatment. It reduces fatigue and improves quality of life.
- Eating a healthy diet can help manage side effects during treatment. Limit alcoholic drinks, red meat and processed foods and eat more plant-based foods, such as fruits, vegetables and legumes.

What questions should I ask my doctor?

You will have your own ideas about things you want to know, but here are some suggestions:

- What is the goal of my treatment? Will it cure my cancer or just slow it down?
- Will my cancer symptoms go away?
- What are my treatment options?
- What drugs will I receive and how do they work?
- What side effects might occur? How long will they last?
- What can I do to prevent or cope with side effects?
- Who should I contact if I develop any side effects?
- Am I eligible to participate in any clinical trials?
- How will my treatment affect my family and my social life?
- Is there anything I can do, such as changing my diet, exercising, or managing stress, to help cope during treatment?
- Who will be in charge of my long-term care?
- How often should I return for follow-up visits?
- What do you look for during follow-up visits?
- Can I be treated closer to home?

Are there any other resources available?

There are several organizations that can provide you with additional information and support. Consider looking online for:

- Bladder Cancer Canada
- Canadian Cancer Society
- Canadian Cancer Survivor Network
- Canadian Urological Association

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