National Comprehensive Cancer Network®

2026

NCCN Guidelines for Patients®

Cancer care recommendations from leading experts at the National Comprehensive Cancer Network® (NCCN®)

Bladder Cancer



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NCCN Guidelines for Patients®

The essential guide for people facing cancer.

Based on care recommendations from leading cancer experts.

Explains high-quality cancer care provided at state-of-the-art cancer centers.

Reviewed and revised every year.

Did you know that top cancer centers across the United States work together to improve cancer care? This alliance of leading cancer centers is called the National Comprehensive Cancer Network® (NCCN®).

Because cancer care is always evolving, NCCN develops and frequently updates evidence-based cancer care recommendations used by health care providers worldwide. These recommendations are known as the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®).

The NCCN Guidelines for Patients plainly explain these expert recommendations, so you can talk with your care team about the best care for you.

These NCCN Guidelines for Patients are based on the NCCN Guidelines® for Bladder Cancer, Version 2.2026 — June 22, 2026.

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1
About bladder cancer

5 What is bladder cancer?

6 What's the best treatment for bladder cancer?

7 How can I get the best care?

Having cancer can make you feel anxious and worried. This guide will help you understand your diagnosis of bladder cancer. It will also explain your options for treatment. Taken together, you'll have the confidence to make well-informed decisions about what's best for you.

What is bladder cancer?

Bladder cancer is a disease where cells in the inner lining of the bladder multiply and grow out of control. It's one of the most common cancers in adults.

Cancer is what happens when something goes wrong with the natural cell process, causing some cells in the bladder to become abnormal. These abnormal cells are cancer cells.

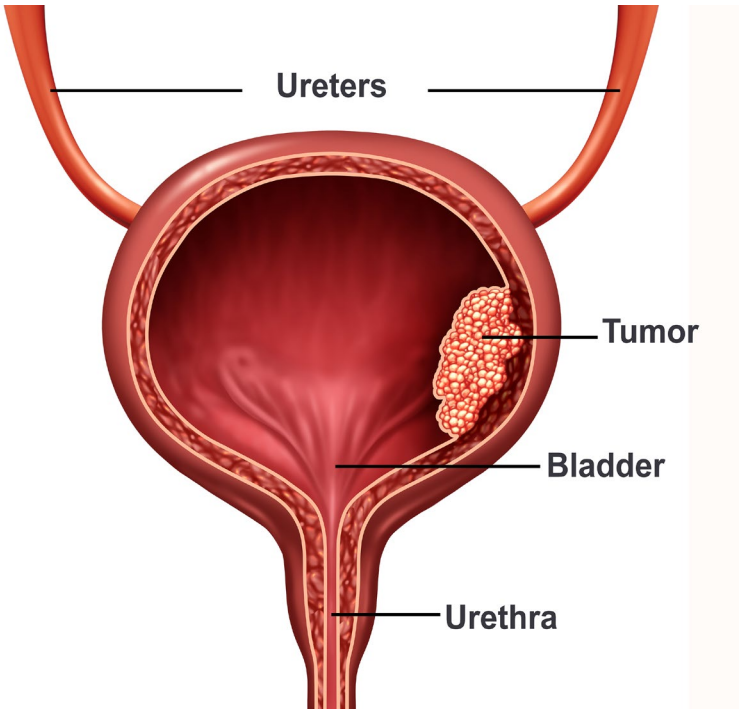
Cancer cells don't behave like ordinary cells. They develop changes that allow them to multiply quickly and make many more cancer cells. Cancer cells crowd out and overwhelm normal cells.

Cancer cells also survive much longer than normal cells do. Over time, cancer cells may form a tumor in the bladder. Sometimes the cells grow deeper and invade the bladder's muscle layer. The cancer may even break through the bladder and spread to other parts of the body. This spreading is called metastasis, or metastatic cancer.

Bladder cancer

Bladder cancer is often described by how far it has spread into the muscle layer of the bladder.

Here, the cancer tumor has grown through the inner lining (urothelial layer) and invaded the muscle layer in the bladder wall. This type of cancer is known as muscle-invasive bladder cancer.



Where does bladder cancer start?

Bladder cancer usually starts in the cells of the bladder's stretchy inner lining, called the urothelium. This lining prevents urine from leaking back into the body.

The bladder's main job is to store urine. It's a hollow, balloon-like organ located in your pelvis—the area between your hip bones in your lower abdomen.

How far along is my bladder cancer?

Once bladder cancer is found, it's important to know how far it has grown or spread. Bladder cancer advances in 4 phases.

- **Non–muscle-invasive bladder cancer** has grown on or into the bladder's inner layer of urothelial cells, but not into the bladder's muscle layer.
- **Muscle-invasive bladder cancer** has grown through the bladder's inner urothelial layer and into its muscle layer. But it hasn't grown anywhere else.
- **Locally advanced bladder cancer** has grown through to the outside of the bladder. It has also reached nearby lymph nodes or organs in the pelvis, but it hasn't spread to organs or lymph nodes far from the bladder. (Lymph nodes are small, bean-shaped glands that transport a fluid called lymph and help fight infection. Lymph nodes are found around the urinary tract and all over the body.)
- **Metastatic bladder cancer** has spread outside the bladder to other areas of the body. Common areas of metastatic bladder cancer include lymph nodes outside the pelvis, bones, lungs, liver, and the inner wall of the abdomen.

Treatment is different for each of these 4 phases of bladder cancer. The phases are further divided into stages, which are explained in *Chapter 3: Staging and grading bladder cancer*.

What's the best treatment for bladder cancer?

No single treatment for bladder cancer is best for everyone. The choice of treatment is based on your cancer stage as well as your overall health and personal preferences.

Very often, the best option includes more than one type of therapy. Common treatments for bladder cancer include:

- Surgery
- Chemotherapy
- Immunotherapy
- Radiation therapy
- Targeted therapy

Surgery, by itself or with other treatments, is used in many stages of bladder cancer. A surgical procedure can remove just the tumor in less advanced cancer or the entire bladder in more advanced cancer.

You may also receive chemotherapy or immunotherapy directly into the bladder. For people with metastatic bladder cancer, chemotherapy or immunotherapy is used to treat cancer anywhere in the body. You can find out more about your treatment options in *Chapter 4: Types of treatment*.

Treatment for any side effects caused by cancer therapy is called supportive care. See *Chapter 8: Supportive care and other assistance*.

How can I get the best care?

Advocate for yourself. You have an important role to play in your care. Many people feel more satisfied when they actively take part in planning their cancer care.

The NCCN Guidelines for Patients will help you play a larger role in your care. Discuss the recommendations in this guide with your care team. Ask questions about your options and share your goals and concerns.

Don't know what to ask? You're not alone. That's why we include suggested questions to ask at the end of chapters.

Keep reading to find the best care for you.

How this guide can help you

Making decisions about cancer care is stressful. There's a lot to learn, and you don't know what the future holds.

Use this guide to get the information and support you need.

Patients, doctors, and other health care professionals trust the NCCN Guidelines for Patients. This guide uses clear, everyday language to explain current cancer care recommendations made by respected experts in the field. Their recommendations are based on the latest research and practices at leading cancer centers.

Your health is unique to you, so your cancer care should be, too. As you read this guide, you'll learn which treatments are likely to provide the best results for you. And you'll be better prepared to talk with your care team.



Try to remember that everyone's journey is different. Your physiological, mental, emotional, and spiritual response is unique."

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Testing for bladder cancer

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Several tests are needed to diagnose and treat bladder cancer. This chapter explains these tests and what to expect during testing.

Before you can be treated, you'll need several tests to confirm your diagnosis. A diagnosis means identifying an illness by using tests. These tests measure how much the cancer has grown and how quickly it's growing.

Tests are also used to plan treatment, to find out how well treatment is working, and to check if the cancer has come back after treatment.

This chapter describes what tests you may have and what to expect during testing. Not everyone will need all of these tests. See **Guide 1**.

Some people reading this guide may have already been tested and given a diagnosis of bladder cancer. For those who haven't been diagnosed yet, the only way to make sure you have bladder cancer is to have tests that:

- Look inside your bladder (cystoscopy and imaging)
- Analyze your urine (urinalysis and cytology)
- Examine a sample of surgically removed bladder tissue (resection and biopsy)

Guide 1
Tests and procedures for bladder cancer

Tests for diagnosis	**General health tests** Medical history Family history Physical exam
	Blood and urine tests • Complete blood count (CBC) • Comprehensive metabolic panel (CMP) • Urine test for biomarkers
	Cystoscopy
	Imaging of bladder • MRI
	Transurethral resection of bladder tumor (TURBT)
Other tests, if needed	**Urine tests** • Urine cytology
	Additional imaging • CT • PET/CT
	Biopsy
	Genetic test for cancer risk

General health tests

Medical and family histories

A medical history is a record of all health issues and treatments you've had in your life. Be prepared to list any illness or injury and when it happened. Also, put together a list of your prescription medications and any over-the-counter medicines, herbals, or supplements you take.

Some cancers and other diseases run in families. Your care team will ask about the health history of family members who are blood relatives. This information is called a family history. Ask your family members about their health issues like heart disease, cancers, and diabetes, and at what age they were diagnosed.

Physical exam

A physical exam is a check of your body for any signs of disease. Your health care provider may feel for abnormalities or tenderness in your abdomen and pelvis.

> **"I quickly learned from my oncologist that he was also a therapist. There's no concern that is too trivial or stupid for them to answer. Their job is so much easier if they know how and what you're feeling."**

Blood and urine tests

Blood tests check for signs of disease and how well organs are working. A blood test requires a sample of your blood. One sample may be used for several different blood tests.

Complete blood count

A complete blood count (CBC) measures the levels of red blood cells, white blood cells, and platelets in your blood. Your provider will want to know if you have enough red blood cells to carry oxygen throughout your body, white blood cells to fight infection, and platelets to control bleeding. Your white blood cell count may be elevated if you have a bladder-related infection or inflammation.

Comprehensive metabolic panel

A comprehensive metabolic panel (CMP) measures important chemicals, proteins, and other substances in your blood. Levels that are too high or low could be a sign of a health problem in the kidneys or liver. For instance, bladder cancer and cancer treatments can affect your kidney function and urine flow.

Some important tests in a CMP are:

- **Liver function test** looks at enzymes made by the liver. Elevated levels may be a sign of liver damage and could affect which treatment you receive.
- **Kidney function test** measures waste products like creatinine and blood urea nitrogen to check if your kidneys are working normally.

Urine cytology

Urine cytology is a lab test that analyzes your urine for cancer or precancerous cells. You may receive a urine cytology test if you have blood in your urine.

A urine cytology is done like other urine tests—you pee into a small plastic container. Or your urologist may collect a sample of your urine during a cystoscopy exam. Either way, the urine sample is sent to a lab for testing. At the lab, a pathologist (a doctor who examines cells and tissue to find disease) will look for abnormal cells in your urine sample.

If abnormal cells are found, it means that cancer may be located anywhere in the urinary tract. You'll need a cystoscopy procedure to find out if it's in the urethra or the bladder. If cancer isn't found in the urethra or bladder, you'll need imaging tests to investigate the ureters, kidneys, and other areas.

Urine tests for tumor markers

Tumors shed cancer cells, which can end up in your urine. Urine tests are now available to identify some of these specific tumor cells. Scientists call these urinary biomarkers.

Biomarker tests may provide some useful clues when bladder cancer is suspected. But at this time, these tests aren't yet reliable enough to diagnose cancer on their own.

Biomarker tests are also sometimes used for surveillance in people who've been treated for non–muscle-invasive bladder cancer. Surveillance means watching to see if the cancer comes back after it has been treated or removed.

If you have symptoms, tell your provider

Bladder cancer is usually found when a person has symptoms. The most common symptom of bladder cancer, and the one that usually appears first, is blood in your urine (hematuria).

How does blood get into urine? Bladder tumors are likely to release a little blood, which mixes with the urine in your bladder. The blood may turn your urine pink or bright red. If there isn't enough blood to be visible, your urine may look normal. But your clinical team can still detect blood by looking at a sample of the urine under a microscope.

Blood in the urine can be caused by many other things besides bladder cancer. So anyone with this symptom should see a health care provider for testing.

Other symptoms of bladder cancer can include:

- Frequent urination
- Urgency to urinate
- Painful urination
- Back pain

Not every person with bladder cancer will have many or all of these symptoms. Some people will have no symptoms.

Cystoscopy and biopsy

Cystoscopy is a procedure to look inside your urethra and bladder for any signs of cancer. This procedure uses a cystoscope, a tube-like instrument with a camera and a light at the end, which is inserted into the urethra and through to the bladder.

Cystoscopy may be done at your urologist's office, a hospital, or a clinic. The procedure takes only a few minutes, it doesn't require general anesthesia, and you can usually go home afterward with minimal symptoms and without a drainage tube.

During a cystoscopy

You'll lie on your back on an exam table. You may be positioned with your feet up and your knees apart.

After lubricating the tip of the urethra (and possibly numbing it with an anesthetic gel), your urologist will slowly insert the cystoscope into the opening of the urethra. This is at the tip of the penis or just in front of the vagina. It may be uncomfortable at first, but it shouldn't be painful. The urologist will then move the cystoscope carefully through the urethra and into the bladder.

If any areas appear suspicious, the urologist may use a small tool on the cystoscope to remove tiny tissue samples for testing (biopsy). If a biopsy can't be done during this visit, you might be scheduled for a separate procedure on another day.

In addition to biopsy samples, the urologist can completely remove very small cancer growths during the cystoscopy. However, if a tumor is found, you'll need to have it removed in an operating room at a clinic or hospital.

Is blue light cystoscopy better?

Cystoscopy commonly uses a white light to see inside the bladder. Some newer cystoscopes now use a blue light. When combined with a special dye injected into the bladder, blue light cystoscopy can identify some tumors a little more distinctly than white light.

Another technology called narrow-band imaging also helps detect tumors more clearly during cystoscopy, but it doesn't require a dye like blue light does.

Blue light cystoscopy and narrow-band imaging appear to detect certain tumors better than standard white light. However, these techniques are still relatively new. Additional research may show whether they could replace white light as the standard detection method or be used instead of or in addition to white light in certain cases.

In a very similar exam, called a ureteroscopy, the cystoscope goes a little farther to examine the upper parts of the urinary tract—the ureters and inner kidneys. A ureteroscopy is done only if something seems abnormal with the ureters or kidneys.

After a cystoscopy

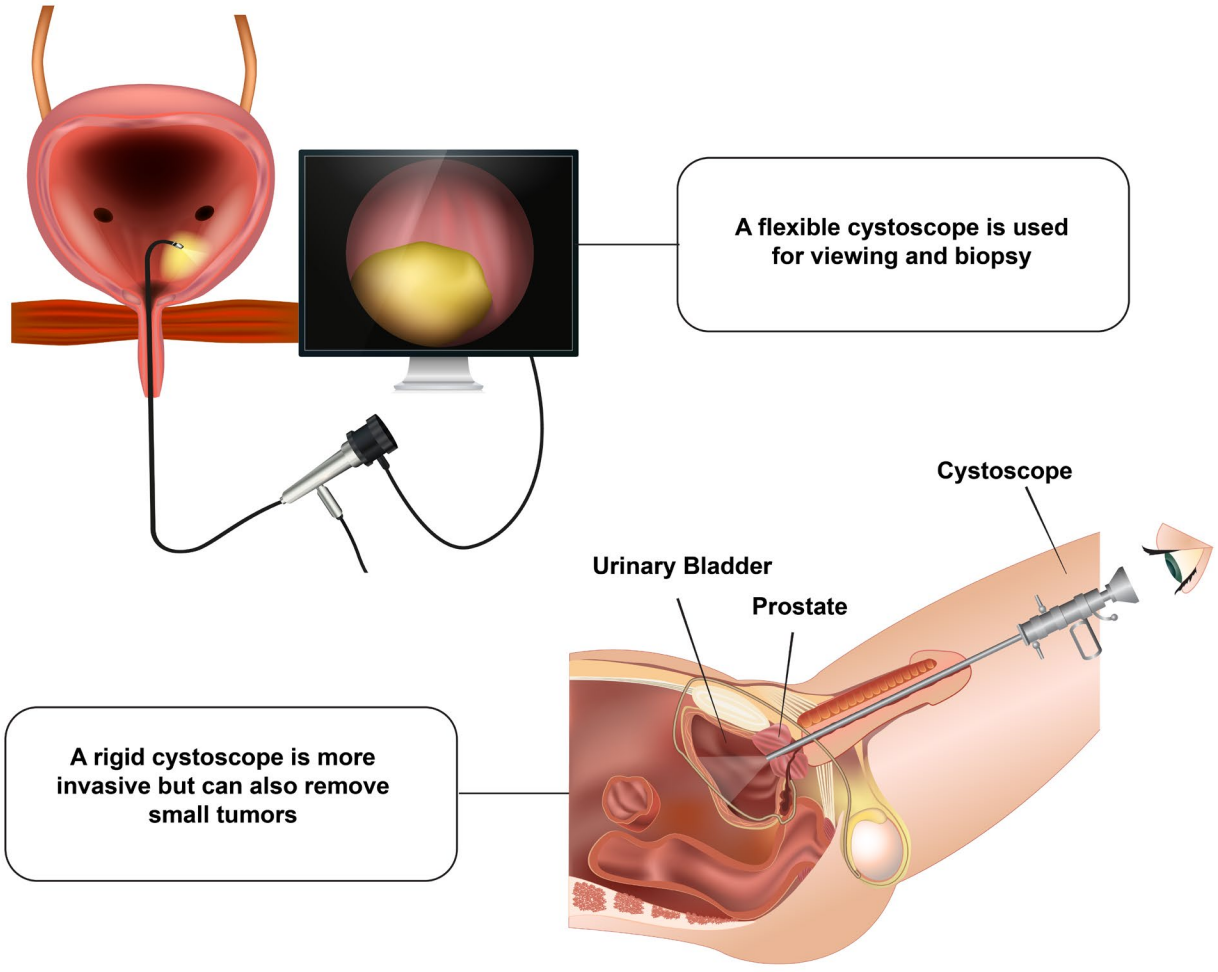
After the procedure, you may have one or more of these side effects:

- Bleeding from your urethra, which can appear bright pink in your urine or occasionally as blood clots on toilet paper
- A burning sensation during urination
- Urinating more often for the next day or two

If a tissue sample was taken for a biopsy, it will be sent to a pathologist at a lab. The pathologist will look for cancer cells and assess how far the cancer has invaded the bladder.

Cystoscopy

A cystoscopy is an exam to look inside the urethra and bladder for any signs of cancer. If anything looks suspicious, the urologist can use a small tool on the cystoscope to remove tiny tissue samples for testing (biopsy). The flexible cystoscope is used more commonly than the rigid kind these days.



Imaging

Imaging means taking detailed pictures (images) of the inside of the body. The images can show the size, location, and other features of cancer. Imaging can reveal where the cancer started and whether it has spread (metastasized).

Types of imaging include x-rays, computed tomography (CT), positron emission tomography (PET), magnetic resonance imaging (MRI), and ultrasound.

CT scan

A CT scan takes many x-rays of the same body part from different angles. A computer combines all the x-rays to make a series of cross-sectional images.

A CT scanner is a large machine that has a round tunnel in the middle. During the test, you'll lie on a table that moves slowly through the tunnel. Pillows or straps may be used to help keep you still during the test.

To look for cancer that has spread beyond the bladder, you may have a CT scan of your abdomen and pelvis. The pelvis is the area of the lower abdomen located between the hip bones. It contains reproductive organs as well as the bladder and rectum.

PET/CT scan

A PET scan uses a radioactive drug injected into a vein to see where cancer cells are in the body. Cancer cells show up as bright spots on PET scans.

When a PET scan is combined with CT, it's called a PET/CT scan. PET/CT creates detailed images that are useful in certain clinical situations for finding cancer that has spread outside the bladder.

MRI

MRI uses radio waves and powerful magnets to take pictures of the inside of the body. An MRI is used to get a more detailed view of cancer within the bladder or urinary tract. It's also used to see if cancer has spread to the liver, nearby lymph nodes, or the bones in your pelvis.

Like a CT scanner, an MRI is a large machine with a round tunnel in the middle. Unlike CT, MRI doesn't use radiation (x-rays). An MRI also makes much more noise and takes longer than a CT scan.

Tell your team if you get nervous in small spaces. You may be given a sedative (medicine) to help you relax. You'll need to remain as motionless as possible during each scan. You may be positioned with pillows or bolsters to help you keep still.

Because an MRI uses magnets, you can't bring any metal objects (such as a mobile phone, wristwatch, belt with a metal buckle, or jewelry) into the imaging room.

Other types of imaging

CT and MRI are commonly used to see how far bladder cancer has spread. Other types of imaging are sometimes used to look for cancer in the rest of the urinary tract or body.

Urogram uses a contrast solution and either CT or MRI to see how well your entire urinary tract is working and if there are any tumors in the upper urinary tract. Contrast makes the lining of your kidneys, ureters, and bladder easier to see. You may have a urogram if

you're feeling symptoms, such as pain in your side or back, or if you have blood in your urine.

Renal ultrasound shows your kidneys, ureters, and bladder in real time. It's the same technology used to look at a baby in the womb. A renal ultrasound is a painless, non-surgical test that produces black-and-white images of your kidneys and other organs.

Pyelogram uses x-rays and contrast solution to look for a blockage—such as a tumor, kidney stone, or blood clot—in your ureters or kidneys. This test may also be used to find causes for blood in urine. A pyelogram is usually done in the operating room during a cystoscopy. You'll be given anesthesia for this procedure. During the cystoscopy, the contrast is given intravenously (into a vein) or injected directly into the ureters.

Chest imaging uses CT or x-rays to see if the cancer has reached the lungs.

Bone scan is done when symptoms suggest that the cancer has spread to bones.

After your scan, your images will be studied by a radiologist. A radiologist is a doctor who's an expert in interpreting imaging tests. The radiologist will send the results to your doctor or care team.

This information helps to plan the next steps of your care. Your doctor or other health care provider will discuss the results with you. Be sure to ask any questions you have.

Tumor removal and testing

After imaging locates the tumor, you'll likely have a procedure that does double duty to:

- Remove some or all of the tumor from the bladder **and**
- Assess the tumor to find out what stage it is. (Staging is discussed in depth in the next chapter.)

Imaging

To look for cancer that has spread beyond the bladder, you may have an imaging scan of your abdomen and pelvis.



Importantly, this procedure doesn't cut into the abdomen or surgically remove the bladder. Instead, the tumor is taken out (resected) through the urethra. Then it's tested to provide a diagnosis.

This procedure is called a **t**rans**u**rethral **r**esection of **b**ladder **t**umor (TURBT, sometimes pronounced tur-bit). You'll be given general anesthesia for the procedure, so you'll be asleep and won't feel any pain or discomfort.

The TURBT procedure itself is explained in *Chapter 4: Types of treatment*.

In terms of testing, the important points to know are:

- TURBT can confirm the cancer diagnosis.
- TURBT can find out if the tumor has or hasn't invaded the bladder's muscle layer.

Examination under anesthesia

While you're under anesthesia for TURBT, another test called an examination under anesthesia is often done at the same time.

The goal of this examination is to feel for any tumors on the **outside** of the bladder. If any tumors are found, this examination can provide information about the size and location of the tumor, and whether it has grown into the bladder's muscle layer.

This information adds to any other evidence gathered for finding out the stage of the tumor. If the bladder is attached to an adjoining organ, that could increase the stage and risks.

Your urologist or other provider will put one hand on your abdomen and, with the other hand, insert a gloved finger into your rectum or vagina. This way, the urologist can physically feel the surface of the bladder with both hands. Other members of the surgical team will be there to assist.

You may or may not undergo this test depending on whether the cancer has reached the outer surface of the bladder (muscle-invasive) and/or whether your provider thinks it's necessary.

Genetic testing for cancer risk

Sometimes, changes (mutations) in genes inherited from your parents can increase the risk of different cancers. You can pass these genes on to your children. Other family members might also carry these mutations.

If you have a family history of cancer, your doctor might suggest genetic testing to find out if you have an inherited cancer risk. This type of genetic testing looks for mutations that occur in every cell in your body.

Genetic testing for inherited mutations may be more appropriate for people who have:

- Already had cancer
- A close relative with bladder cancer
- Age below 50
- Cancer of the upper urinary tract
- High-grade (fast-growing) cancer
- Lynch syndrome or a family member with Lynch syndrome

Inherited mutations are not a common cause of bladder cancer. But if you have one or more of these factors, you should ask about genetic counseling. A genetic counselor is an expert who has special training in genetic diseases and can help you decide whether to have genetic testing.

If you have an inherited risk, such as Lynch syndrome, you might require additional testing or specialized treatment.

The test is done using a sample of your blood, saliva, urine, or tumor tissue. A genetic counselor will also help you interpret the results of these tests.

Quitting smoking

Smoking increases the risk of bladder cancer. The more you smoke, the greater your risk. Smoking also interferes with cancer treatment and surgery, making it less effective and more risky. Quitting smoking isn't easy. But it could reduce your risk of other cancers or serious diseases.

Key points

- A diagnosis means identifying an illness by using tests.
- Tests of your blood and urine can show if something in your body isn't working right. This may be a clue that you have a serious illness, such as cancer.
- Cystoscopy uses a viewing device inserted through the urethra to look for cancer inside the bladder.
- Imaging tests can show whether cancer has spread to tissues, organs, and lymph nodes near the bladder or to distant parts of the body.
- People who smoke are much more likely to die of bladder cancer than those who don't smoke.

Questions to ask

- Where do I go for testing, and how long will it take?
- How often are these tests wrong?
- How soon will I know the results and who will explain them to me?
- How can I get a copy of the pathology report and other test results?
- Who will talk to me about the next steps?

3

Staging and grading bladder cancer

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The stage and grade of your cancer represent how far and how fast it has grown. Your care team needs to know the stage and the grade of your cancer to predict the course of your disease and to make a treatment plan.

How far and how fast?

You've had many tests to learn about your cancer. But before you receive treatment, your care team needs to figure out how far your cancer has grown and how fast it's growing. This is done with staging and grading.

Stage measures the physical extent of the cancer. It's a number rating of how far the cancer has grown into the bladder wall. Numbers range from 0 to 4, where 0 means no growth into the bladder wall and 4 means growth through the bladder wall and into other parts of the body.

Grade measures the overall aggressiveness of the cancer. It's an estimate of the rate that the cancer is growing. Cancer grade is either low grade (slow) or high grade (fast).

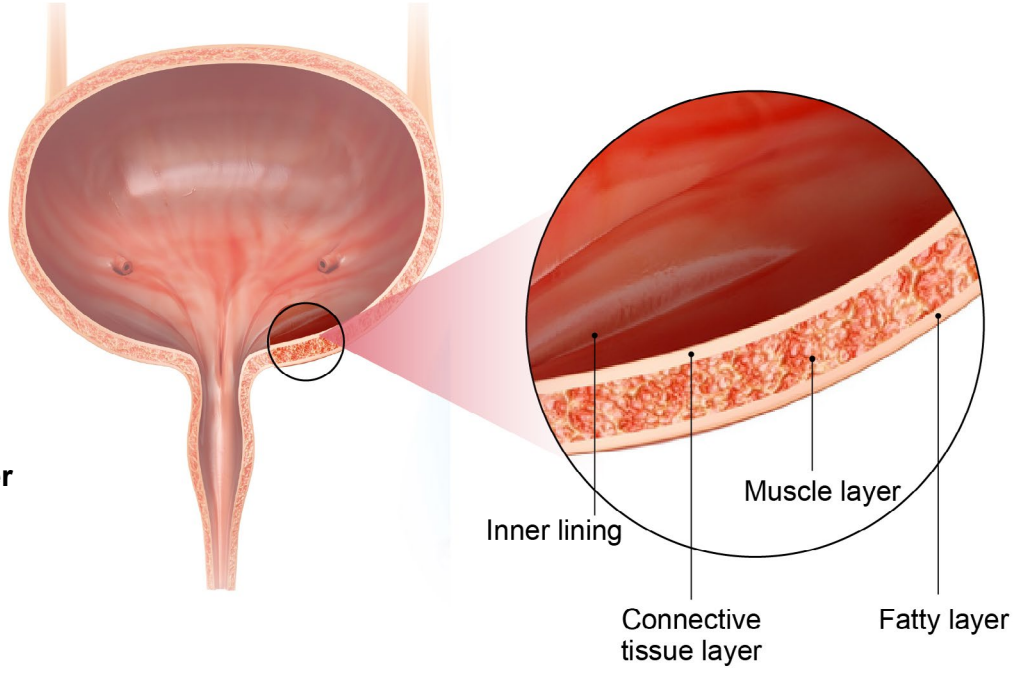
It's important for your care team to know the stage and grade of your cancer to predict the course of your disease and to make a treatment plan.

The next chapters explain how these ratings are used to choose treatments. But first, let's get to know more about staging and grading.

Layers of the bladder

The wall of the bladder has 4 main layers. From the inside to the outside, they are:

- **Inner lining (urothelial layer)**
- **Connective tissue layer**
- **Muscle layer**
- **Outer fatty layer**



Stage

Staging is a way to describe how much cancer is in your body, how much it has grown, and how far it has spread.

If the cancer has spread outside the bladder (metastasized), staging describes where it has spread to and whether it's affecting other parts of the body.

Staging uses your test results to identify and locate your cancer. Staging helps you and your care team select the best therapy.

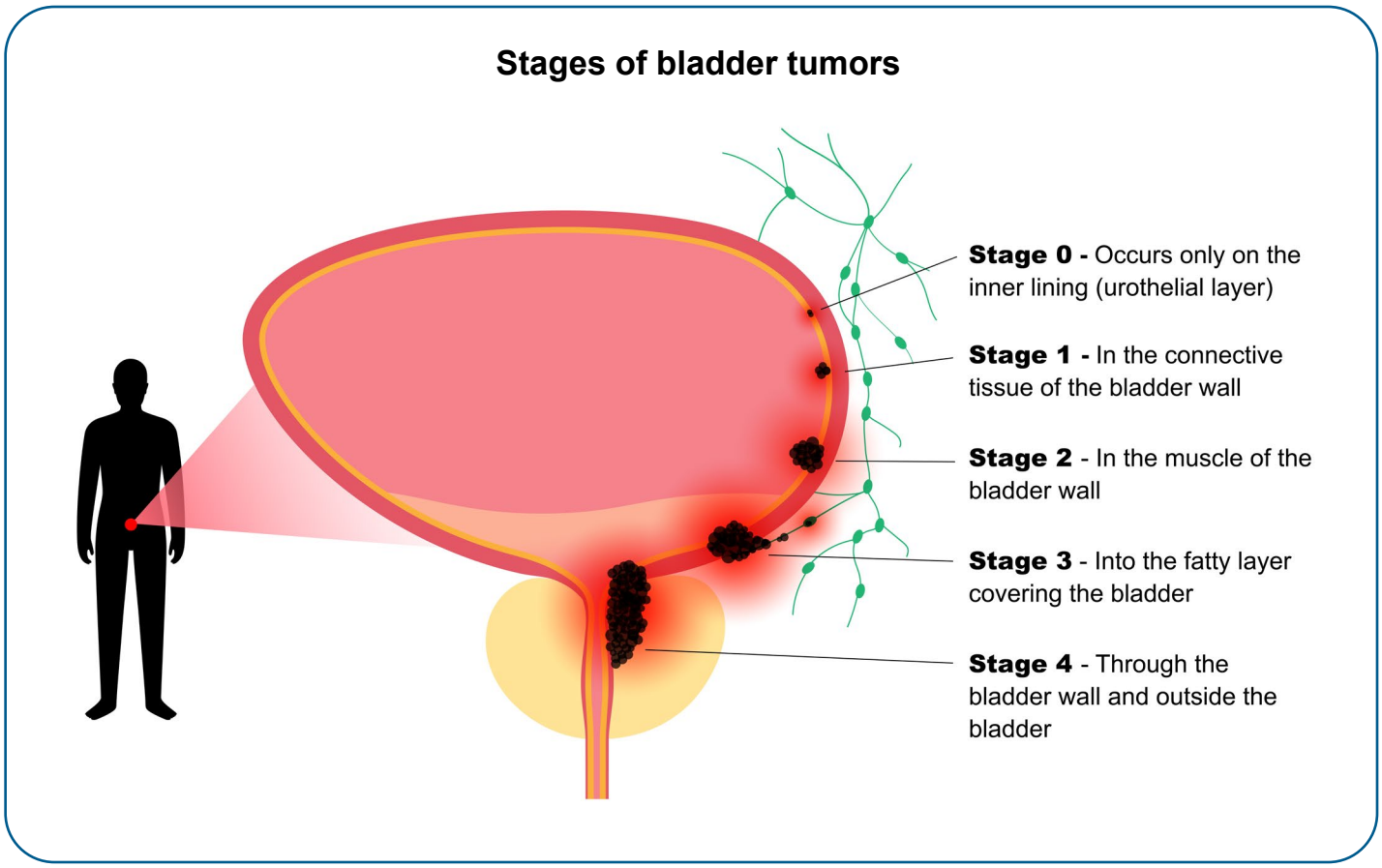
There are five stages of bladder cancer: 0, 1, 2, 3, and 4. Some stages are also divided into subgroups.

You may see the cancer stage written with a T, where the T stands for tumor: T0, T1, T2, T3, and T4.

Muscle-invasive or non–muscle-invasive?

An important thing about bladder cancer is whether the tumor has or hasn't grown into the layer of bladder muscle. Stage 0 and stage 1 cancers haven't grown into the muscle layer (non–muscle-invasive). Bladder cancer is often found in these early stages, when it's highly treatable.

Cancers in stages 2, 3, and 4 have grown into the muscle layer (muscle-invasive). Cancer that has invaded the muscle layer needs more intense treatment.



Stage 0

Stage 0 is the earliest stage of bladder cancer. This stage of cancer affects only the inner lining of the bladder (urothelial layer). Stage 0 has two subgroups:

- **Stage 0a** describes cancer cells that grow from the inner lining toward the hollow center of the bladder, rather than into the bladder wall.
- **Stage 0is** stands for carcinoma in situ (CIS). This is a flat patch of cancer cells that hasn't grown any farther than where it started. It's still on the surface of the bladder lining and has yet to invade deeper layers. However, CIS is fast-growing and can be very serious.

Stage 1

Stage 1 has grown through the inner lining of the bladder wall and into the layer of connective tissue. But stage 1 hasn't invaded the muscle layer of the bladder wall (non–muscle-invasive).

Stage 2

Stage 2 bladder cancer has grown into the muscle layer (muscle-invasive), but it hasn't reached the fatty layer covering the outside of the bladder, nor has it spread anywhere else.

Stage 3

Stage 3 has grown through the bladder wall and into the fatty layer surrounding the bladder. It may also have spread to nearby (in the pelvis) lymph nodes and organs.

Stage 3 bladder cancer has two subgroups:

- **Stage 3A** bladder cancer may only be in the fatty tissue surrounding the bladder, or it may have spread to a single nearby lymph node. It may also invade nearby reproductive organs, such as the prostate gland, uterus, or vagina. Stage 3A cancer has not spread to nodes or organs far from the bladder.
- **Stage 3B** has the same traits as stage 3A but has spread to multiple lymph nodes near the bladder. Stage 3B cancer has not spread to lymph nodes or organs far from the bladder, so it's called locally advanced bladder cancer.

Stage 4

Stage 4 cancer has grown through the bladder wall and may have spread to lymph nodes or organs near or far from the bladder.

Stage 4 bladder cancer has two subgroups:

- **Stage 4A** has invaded the wall of the pelvis or abdomen. Or it has spread to nearby lymph nodes. So it's considered locally advanced bladder cancer.
- **Stage 4B** has spread to a distant organ (or organs) like the liver, lungs, and bones. It may also have spread to nearby lymph nodes and organs. Stage 4B is metastatic bladder cancer.

Come armed to each and every appointment with all of your questions and concerns—and do not leave until you get them all answered!"

Grade

The next piece of information used to plan treatment is the cancer grade. The grade measures how aggressive the cancer is. It's a rating of how fast the cancer will likely grow and spread.

To figure out the grade, a sample of your tumor will be studied in a laboratory by a pathologist. The pathologist will compare the cancer cells to normal cells. The more different they look, the higher the grade. And the higher the grade, the faster the cancer is expected to spread.

- **LG** means that the cancer cells are low grade (slow growing).
- **HG** means that the cancer cells are high grade (fast growing).

Subtypes

The inner lining of the bladder is made of urothelial cells. Most cases of bladder cancer start in the urothelial cells. So this type of cancer is called urothelial cancer.

But in rare cases, urothelial cancer has features that look like other types of cells. These are called subtypes. Some of them include:

- Glandular subtype
- Squamous cell subtype
- Micropapillary subtype
- Plasmacytoid subtype
- Sarcomatoid subtype
- Lymphoepithelioma-like subtype
- Microcystic and tubular subtype

It's important to investigate whether you have one of these or another subtype. In general, treatment for these uncommon subtypes in the early stages is similar to treatment for typical urothelial cancer.

However, some subtypes might grow or advance faster than typical urothelial cell cancer. And faster growth might mean your cancer needs more aggressive treatment.

Key points

- The stage of cancer describes how deep it has grown into the bladder wall and how far it has spread.
- Bladder cancer at stage 0 and stage 1 hasn't invaded the muscle layer. Bladder cancer is often found at one of these early stages, when it's highly treatable.
- Stages 2, 3, and 4 bladder cancers have invaded the muscle layer of the bladder wall (muscle-invasive). Cancer that has invaded the muscle needs more aggressive treatment.
- In stage 3 bladder cancer, the tumor has grown into the fat layer around the bladder. There may also be cancer in nearby lymph nodes.
- Stage 4 is locally advanced or metastatic bladder cancer. This is cancer that has grown outside the bladder and has spread to other areas in the body.
- Cancer grade is an estimate of how fast the cancer is expected to grow. Low-grade bladder cancer is slow growing. High-grade cancer grows more quickly.

Questions to ask

- What is my cancer stage?
- Has the cancer grown into the muscle layer of the bladder wall?
- If the cancer has spread outside the bladder, how far has it spread?
- Can my type of bladder cancer be cured? If not, how well can treatment stop it from growing?

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This chapter explains the different treatment options for bladder cancer. Many people with bladder cancer receive more than one type of treatment. You and your care team will choose a treatment plan that's right for you.

Treatment for bladder cancer is based on many things, including the extent, severity, and type of cancer. It also includes your age, your ability to perform daily tasks, your other health issues, and the availability and affordability of drugs. Importantly, treatment is also based on your wishes and preferences.

There are several ways to treat bladder cancer. It's likely that you'll need a few different types of treatment over months or years.

This chapter explains all the different treatments. The chapters after this one describe treatments for each stage of bladder cancer.

Treatments include:

Surgery – The goal of surgery is to take out the tumor and sometimes the surrounding tissue. Surgery procedures range from snipping a single tumor from the bladder lining to removing the entire bladder and other organs.

Intravesical therapy – Intravesical therapy involves filling the bladder with a liquid medication that helps destroy cancer cells.

Systemic therapy – Systemic therapy is typically an intravenous (IV) treatment that treats cancer anywhere in the whole body. Types of systemic therapy include chemotherapy, immunotherapy, and targeted therapy.

Radiation therapy – Radiation therapy uses high-energy rays to kill cancer cells. Sometimes chemotherapy or another therapy is added to radiation therapy to enhance treatment.

Clinical trial – Clinical trials are done to test experimental treatments. You may be able to join a clinical trial at any time.

Surgery

Types of surgery for bladder cancer include tumor removal and bladder removal.

Tumor removal

For bladder cancer, a surgical procedure called a resection removes the tumor but leaves the rest of the bladder in place. The full name of the procedure is called a **t**rans**u**rethral **r**esection of **b**ladder **t**umor (TURBT, sometimes pronounced tur-bit).

Even though it has a complicated name, the concept of TURBT is simple. The procedure removes tumors through the urethra without having to cut into the abdomen. The tumor can then be tested to provide a diagnosis.

TURBT is done in an operating room in a clinic or hospital. You'll be given anesthesia that puts you to sleep. The urologist then guides an instrument with a small cutting device through the urethra and into the bladder. The instrument is used to examine and remove the tumor from the bladder lining.

The goals of TURBT are to:

- Confirm the initial bladder cancer diagnosis.
- Remove all the visible tumor.
- Take a sample of the bladder wall to see if the tumor has invaded the muscle layer.

While you're under anesthesia, another test called an examination under anesthesia may also be done. For more information on this procedure, look for it in *Chapter 2: Testing for bladder cancer*.

After the procedure, most people can go home the same day. But you'll still need a few more days to rest and recover. You may feel pain or burning when you urinate and have blood in your urine for the following 2 to 4 weeks or so.

Another TURBT procedure may be needed about 2 to 6 weeks after the first one. The second TURBT is done to make sure all the tumor is removed.

A treatment called intravesical therapy may be done in combination with TURBT. (More about intravesical therapy to follow.)

Bladder removal

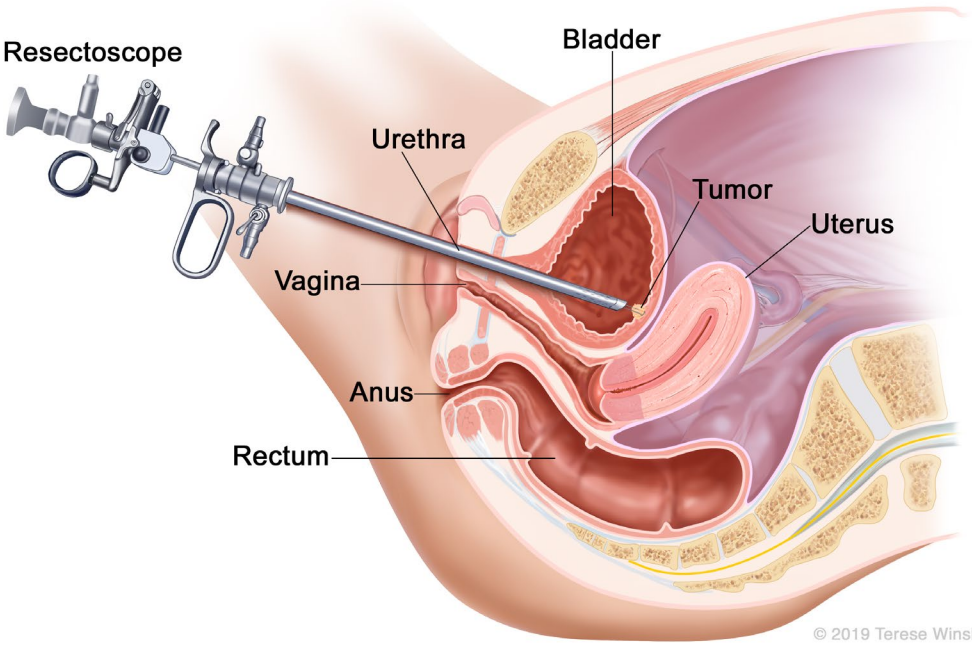
A procedure called a cystectomy treats bladder cancer by removing the entire bladder. It's the most widely used surgery for muscle-invasive bladder cancer.

When it's called a radical cystectomy, that means taking out the entire bladder as well as the surrounding fat and nearby lymph nodes.

Other nearby organs may also be removed. These include the prostate and seminal vesicles (glands that help make semen) in males. In females, part of the urethra, uterus,

TURBT

A transurethral resection of bladder tumor (TURBT) is a procedure that examines and removes tumors on the bladder wall.



cervix, ovaries, and fallopian tubes may also be removed during the procedure. Your surgeon should discuss this with you when developing a treatment plan.

Because a radical cystectomy removes your entire bladder, you'll need a new way for urine to exit your body. So another procedure, called a urinary diversion, is done at the same time. A urinary diversion uses a segment of your small intestine to connect your kidneys to an opening on the outside of your body, which allows you to get rid of urine.

To find out about the 3 types of urinary diversion, see page 28.

A radical cystectomy is a major operation that involves cutting into your abdomen. You'll need to stay in the hospital for several days. It may take 2 to 3 months or longer for you to recover.

Common side effects and complications of a radical cystectomy include constipation, diarrhea, bleeding, bowel problems, infections, and changes in sexual function.

Talk to your urologist and treatment team about the risks, benefits, and side effects of a radical cystectomy.

Partial cystectomy

A partial cystectomy is a surgical procedure to remove part of the bladder. It's not widely used to treat bladder cancer because few people are eligible for it.

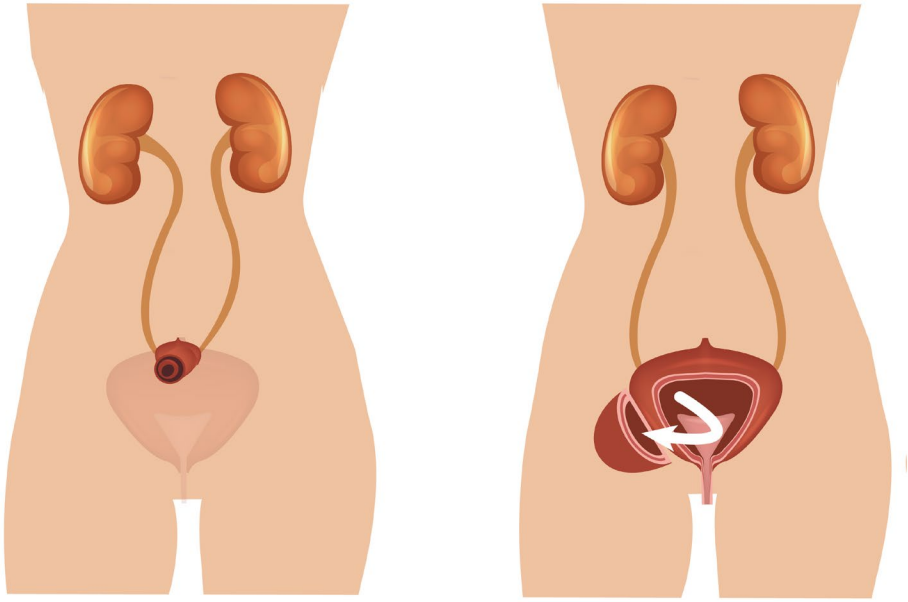
A partial cystectomy can only be done if the cancer is in a spot that can be neatly removed without taking out the whole bladder.

Cystectomy

Cystectomy is surgery to remove the bladder.

A radical cystectomy removes the entire bladder, nearby lymph nodes, and other organs. It's the most common surgery for muscle-invasive bladder cancer.

A partial cystectomy removes part of the bladder. It's rarely used for bladder cancer.



Radical Cystecomy | Partial Cystecomy



Types of urinary diversion

If your bladder is removed, urine needs another way to leave your body. This requires an additional surgical procedure called a urinary diversion. There are 3 types of urinary diversions.

Ileal conduit

In this urinary diversion, the surgeon adapts a section of the small intestine (ileum) to use as a tube (or conduit). The surgeon also creates a small hole, called a stoma, in the abdominal wall. One end of the tube is connected to the ureters, much like the bladder was. The other end of the tube is used to create the stoma. Urine drains from the kidneys and ureters, passes through the tube, and exits the body through the stoma.

Urine can trickle out of the stoma at any time. A small disposable bag is attached to the outside of your abdomen to collect the urine when it comes out of the stoma. This is called an ostomy bag (or ostomy pouch). The bag is attached to your body with the help of an adhesive ring. The ring sticks to the skin and acts as a watertight barrier.

Most people find that they need to empty the bag every 2 to 4 hours, depending on how much liquid they drink. A closable spout at the bottom of the bag allows the urine to be emptied into a toilet without taking off the bag.

Neobladder

For this procedure, the bladder is replaced with a segment of small intestine that acts like a new bladder (neobladder).

Like the original bladder, this substitute bladder is attached to the ureters at one end and to the urethra at the other end. This means that urine follows the same path out of the body it normally would if you still had your bladder. Because urine leaves the body in the usual way, a stoma and an ostomy bag aren't needed.

A neobladder doesn't work exactly the same way as a real bladder. You'll probably need to empty it more often at first, maybe every 1 to 3 hours.

Also, urine might come out when you don't want or expect it to, like during sleep. This is called urinary incontinence. With time and training, you'll be able to better control the flow of urine from your neobladder. Even so, a neobladder may be difficult to empty completely. Some people have a catheter inserted through their urethra to help empty the neobladder.

Continent cutaneous pouch (Indiana pouch)

This urinary diversion uses a portion of the large intestine to create a pouch to hold urine. (It's also called an Indiana pouch because it was developed by surgeons at Indiana University.)

A section of the small intestine is used to connect the pouch to a stoma in the wall of the abdomen. A one-way valve, made from part of the intestine, prevents the urine from flowing out of the stoma.

The stoma can be covered by a small bandage. A catheter must be inserted into the stoma, through the valve, and into the pouch several times a day to drain the urine. Sometimes the stoma can be made in the belly button, making it less noticeable.

A benefit to this type of urinary diversion is that no ostomy bag is needed. This may appeal to people with concerns about body image or people who don't want to worry about the bag coming loose or leaking.

Intravesical therapy

While surgery is done to remove visible cancer, intravesical therapy is used to destroy cancer cells that aren't visible or are hard to reach.

Intravesical therapy means putting medicine directly into the bladder. It's done with a flexible tube, called a catheter, inserted into the urethra. The medicine flows through the catheter and into the bladder.

The two main intravesical therapies used to treat bladder cancer are bacillus Calmette-Guérin (BCG) and chemotherapy.

Intravesical BCG

Intravesical BCG therapy uses a fluid that contains a very weak bacterium (germ). The germ triggers the immune system, causing the immune system to attack cancer cells inside the bladder.

Destroying these cancer cells can lower the chance of recurrence (cancer coming back) or getting worse (invading bladder muscle).

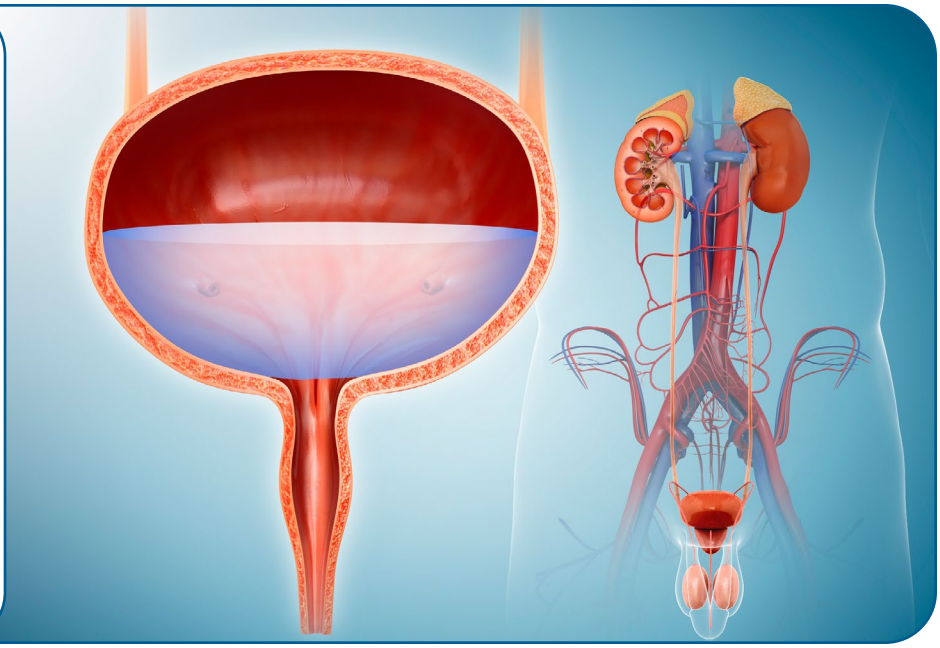
Intravesical BCG is commonly used for bladder cancer that hasn't invaded the muscle layer. It's usually started about 3 to 6 weeks after TURBT, to allow the bladder time to heal. It's given once a week for 6 weeks. You should have a full re-evaluation at 12 weeks after starting treatment.

To prevent recurrence, you might be asked to continue having intravesical BCG therapy. This is called maintenance therapy. Maintenance therapy involves intravesical BCG treatments given 3 months after TURBT and again at 6 months. You may continue to have maintenance therapy every 6 months for up to 3 years, depending on the risk of recurrence.

Possible side effects of intravesical BCG therapy include fever, chills, the urge to urinate, pain, or difficulty when urinating as well as blood or particles (clots) in your urine.

Intravesical therapy

Intravesical therapy is a treatment where a liquid medicine is placed directly into the bladder. The medicine aims to destroy any cancer cells that TURBT left behind and to prevent any new cancer cells from forming.



Talk to your treatment team about the side effects. There may be ways to help lessen them.

If intravesical BCG doesn't work on its own, a number of other treatment options are available, including treatment in clinical trials.

Intravesical chemotherapy

Chemotherapy is a drug used to kill actively growing cancer cells. Intravesical chemotherapy is given to treat the cancer in the bladder and to reduce the risk of cancer recurrence.

Intravesical chemotherapy can be given soon after a TURBT procedure. The treatment is a one-time dose instilled within 24 hours of TURBT surgery. It's meant to wipe out any cancer cells that surgery may have left behind and to prevent any new cancer from growing.

Intravesical chemotherapy may also be an option if BCG is unavailable, or if you had BCG therapy but it wasn't effective. In these cases, it's given on the same schedule as BCG therapy: once a week for 6 weeks, usually beginning 3 to 4 weeks after TURBT. If you're having maintenance intravesical chemotherapy, it's usually given on a monthly basis for 1 to 2 years.

After the chemotherapy is injected into your bladder, you'll hold it in for 1 to 2 hours. The medicine will empty out of your bladder harmlessly when you pee.

Because intravesical chemotherapy only goes into the bladder and not the entire body, it doesn't usually cause the harsh side effects that chemotherapy is known for. However, it may cause the same type of side effects as intravesical BCG therapy.

The most common intravesical chemotherapies used for bladder cancer are gemcitabine and mitomycin. An intravesical treatment of gemcitabine and docetaxel given back-to-back is also used.

A new way to use gemcitabine is with the **gemcitabine intravesical system (Inlexzo)**. In this technique, a tiny tube filled with gemcitabine is injected into the bladder. Once inside, the tube unfolds into a pretzel-like shape. It remains there for 3 weeks, slowly releasing the chemotherapy over a much longer time than usual intravesical chemotherapy.

After the treatment, the tube is removed from the bladder. Additional tubes can be injected for further treatments.

Currently, the gemcitabine intravesical system is used only for people with carcinoma in situ (stage 0is) bladder cancer who had intravesical BCG therapy that didn't work.

Other intravesical therapies

Two other intravesical therapies are available if intravesical BCG didn't work. They're only given for certain types of high-risk non-muscle invasive bladder cancer.

Nogapendekin alfa inbakicept (Anktiva) is an intravesical immunotherapy that's given together with BCG. Once inside the bladder, it activates immune cells called natural killer cells and T cells.

Natural killer cells, as their name suggests, are good at quickly finding and killing cancer cells. T cells are activated to target specific cancer cells.

Nogapendekin alfa inbakicept also boosts BCG's immune response against cancer cells. It's given along with intravesical BCG once a week for 6 weeks.

Nadofaragene firadenovec (Adstiladrin) is a type of gene therapy that triggers bladder cells to produce interferon alfa-2b, a cancer-fighting protein. Interferon alfa-2b stimulates the immune system to better fight and destroy cancer cells.

Because nadofaragene firadenovec has a prolonged effect in the bladder, it can be given once every 3 months.

Is an end to the BCG shortage in sight?

Even though BCG has been used for decades to treat bladder cancer, it's been in short supply in the United States and worldwide for more than a decade.

As a result, many people with non–muscle-invasive bladder cancer haven't been able to receive this treatment or have received reduced doses. Patients with the highest risk are given the first opportunity to receive it.

If a regular course of BCG treatment isn't available to you, your treatment team may offer intravesical treatment with chemotherapy instead.

Other options include:

- ✓ Reduced doses or a shorter course of BCG treatment
- ✓ Eliminating BCG maintenance therapy
- ✓ Radical cystectomy (for those at high risk of the cancer returning after treatment)
- ✓ Joining a clinical trial, if available

On the upside, the supply of BCG may finally increase in the next few years if all goes according to plan. The world's leading manufacturer of BCG expects its output to triple when its new larger manufacturing plant begins production later this year.

Still, it might take a while for the supply of BCG to catch up with the pent-up demand.

Systemic therapy

Systemic therapy means a treatment that affects the whole body. It's generally given directly into a vein (intravenously, or IV). The most common types of systemic therapy for bladder cancer are chemotherapy and immunotherapy.

To determine which type of systemic therapy is best for you, your treatment team will consider your overall health. This includes how your heart, liver, and kidneys are functioning; how far the cancer has progressed; and your ability to do day-to-day activities.

NCCN levels of preference

All treatments listed in this guide are recommended and appropriate. When helpful, NCCN experts also assign a level of preference to their recommendations for systemic therapies:

- **Preferred therapies** have the most evidence they may work better and be safer than other therapies.
- **Other recommended therapies** can provide effective results but may have less evidence, more side effects, or may not work quite as well as preferred therapies.
- **Therapies used in certain cases** work best for individuals with specific cancer features or health circumstances.

These levels of preference are noted in the next sections.

Note that **systemic** chemotherapy is different from **intravesical** chemotherapy. Intravesical chemotherapy treats the inside of the bladder. Systemic chemotherapy can treat cancer throughout the whole body.

What is dose-dense chemotherapy?

The term dose-dense refers to a method of speeding up chemotherapy by shortening the amount of time between treatments (doses).

The most common systemic chemotherapy used to treat bladder cancer is a combination of medicines known as dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin (or ddMVAC).

Chemotherapy

Chemotherapy is treatment with drugs to kill cancer cells. Most systemic chemotherapy drugs are liquids that are slowly injected into a vein (infusion). The drugs travel in your bloodstream to treat cancer throughout your body.

Chemotherapy may also harm some healthy cells, which is why it can cause harsh side effects. Talk to your care team about any potential side effects from your chemotherapy treatment.

Chemotherapy may be given before surgery to shrink the tumor, and sometimes with immunotherapy both before and after surgery, depending on your type or stage of bladder cancer. Chemotherapy alone (without surgery) is sometimes the main treatment for people who have metastatic bladder cancer.

A commonly used systemic chemotherapy for bladder cancer is cisplatin, which contains the metal platinum. Platinum-based chemotherapy medicines can be effective against bladder cancer but can also damage the kidneys. People with kidney conditions or other health issues may not be able to have chemotherapy or, if possible, may receive non-platinum chemotherapy medicine.

Chemotherapy is given in a sequence of treatments called a cycle. One cycle includes a period of treatments (such as once a day for a few days) followed by a time of rest (several days or weeks). This cycle is then repeated a few times. For example, you might have 3 to 6 cycles of chemotherapy over 2 to 3 months.

Systemic chemotherapies used for bladder cancer include:

- Cisplatin
- Methotrexate
- Vinblastine
- Doxorubicin
- Gemcitabine

Targeted therapy

Targeted therapy is a systemic treatment that can pick out and attack certain types of cancer cells. Targeted therapy is more often used for people with specific gene mutations. If you don't have the mutation that the medicine targets, this treatment is unlikely to help.

A type of targeted therapy called an antibody-drug conjugate combines 2 drugs in 1 medicine. One drug finds and binds to specific cancer cells, and then the other drug attacks the cancer.

Targeted therapies for certain types of bladder cancer include.

- Enfortumab vedotin (Padcev) is an antibody-drug conjugate that targets and attaches itself to a specific protein, nectin-4, found on the surface of bladder cancer cells. Once the drug is attached, it releases a chemotherapy medicine to kill the cancer cell. It's sometimes referred to as a targeted chemotherapy.
- Erdafitinib (Balversa) is a biomarker-targeted therapy used for people whose bladder cancer is due to specific mutations in the *FGFR3* gene.
- Trastuzumab deruxtecan (Enhertu) is a biomarker-targeted therapy as well as an antibody-drug conjugate that targets the HER2 protein on cancer cells. Once it latches onto a cancer cell, it releases a medicine that causes the cell to self-destruct.

Notably, the preferred therapy for metastatic bladder cancer is a combination of targeted chemotherapy (enfortumab vedotin) and an immunotherapy (pembrolizumab).

Because targeted therapy doesn't harm normal cells as much as standard chemotherapy, the side effects tend to be different.

Immunotherapy

Immunotherapy is a type of systemic therapy that uses your immune system to find and destroy cancer cells. The immune system is your body's natural defense against infection and disease.

Checkpoint inhibitors

Checkpoint inhibitors are one type of immunotherapy used to treat bladder cancer and other cancers.

A checkpoint is natural protective action within immune cells. Cancer cells hijack this action to disable immune cells. Checkpoint inhibitors are drugs that block this hijacking tactic, so your immune system can get back to fighting cancer cells.

Checkpoint inhibitors for bladder cancer include:

- Pembrolizumab (Keytruda)
- Nivolumab (Opdivo)
- Avelumab (Bavencio)
- Atezolizumab (Tecentriq)
- Durvalumab (Imfinzi)

Radiation therapy

Radiation therapy uses high-energy waves—such as x-rays—to kill cancer cells and shrink tumors. The type of radiation therapy usually used for bladder cancer is called external beam radiation therapy (EBRT). In EBRT, a large machine aims radiation precisely at the tumor area.

Radiation therapy can be given alone but is more often given with other bladder cancer treatments, such as chemoradiation or trimodal therapy.

Chemoradiation

Chemotherapy and radiation therapy are often used together to treat bladder cancer. This is called chemoradiation or chemoradiotherapy. When given together, they work better than they do alone. Like many cancer treatments, chemoradiation works better for some people than for others.

Trimodal therapy

Trimodal therapy refers to a combination of 3 treatments: TURBT to remove all visible cancer, followed by radiation and chemotherapy given together (chemoradiation).

In certain people with bladder cancer, trimodal therapy can be used instead of a radical cystectomy (bladder removal surgery). This is why trimodal therapy is referred to as bladder-preserving treatment.

Clinical trials

Another way to get treatment is by joining a clinical trial.

A clinical trial is a type of medical research study. After being developed and tested in a lab, potential new ways of fighting cancer need to be studied in people.

If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. FDA.

Everyone with cancer should carefully consider all of the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

Phases

Most cancer clinical trials focus on treatment and are done in phases.

- **Phase 1** trials study the safety and side effects of an investigational drug or treatment approach.
- **Phase 2** trials study how well the drug or approach works against a specific type of cancer.
- **Phase 3** trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase 4** trials study the safety and benefit of an FDA-approved treatment.

Who can enroll?

It depends on the clinical trial's rules, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. They ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

Clinical trials are managed by a research team. This group of experts will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and



Finding a clinical trial

In the United States

NCCN Cancer Centers
NCCN.org/cancercenters

The National Cancer Institute (NCI)
cancer.gov/about-cancer/treatment/clinical-trials/search

Worldwide

The U.S. National Library of Medicine (NLM)
clinicaltrials.gov

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)
1.800.4.CANCER (1.800.422.6237)
cancer.gov/contact

ask questions before signing it. Take time to discuss it with people you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo with a standard treatment, or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

Are clinical trials free?

There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. But you may need to pay for other services, like transportation or childcare, due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is often covered by insurance.

Side effects of treatment

A side effect is an unhealthy or unpleasant physical or emotional condition caused by treatment. All treatments for bladder cancer can cause side effects.

Some people have many side effects while others have few. Some side effects can be very serious. Others are simply unpleasant. Most side effects appear soon after treatment starts and go away after treatment ends. Other side effects are long-term or may appear years later.

Side effects depend on many factors, especially the type, length, and dose of treatment.

Here are some common side effects of different treatments.

Radical cystectomy – Bleeding, blood clots, kidney problems, infection, sexual dysfunction, incontinence, problems caused by the urinary diversion

As a result of clinical trials, many new treatments for bladder cancer have been approved or are on the horizon. As always, you can try to join a clinical trial at almost any point during cancer care.



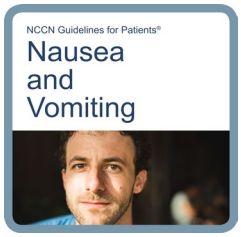
Intravesical therapy – Irritation (inflammation) of the bladder lining, frequent urination, pain or burning feeling when urinating, blood in the urine, infection

Chemotherapy – Nausea, vomiting, extreme tiredness (fatigue), fever, infection, tingling or numbness in fingers and toes, rash, diarrhea

Immunotherapy – Autoimmune reaction (when the immune system mistakenly attacks healthy cells), fatigue, fever, nausea, loss of appetite, infection, diarrhea, constipation

Not every patient develops nausea or vomiting from cancer therapy. But if you have these side effects, it's important to reduce them as much as possible to prevent them from interfering with your treatment.

Read more about these side effects in *NCCN Guidelines for Patients: Nausea and Vomiting*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Other notable side effects

Some side effects happen more commonly in people with bladder cancer, particularly after bladder cancer surgery. While you may not get these side effects, you should be aware of them as you consider the benefits and risks of different treatments.

Sexual dysfunction – Cancer or its treatment may interfere with your ability to have sex. Sexual dysfunction also includes a decreased desire to have sex. This may be due to a lack of energy, being self-conscious about your body after surgery, or feeling stressed out and depressed.

Trouble controlling the flow of urine – Urine may come out when you're not expecting it. This is referred to as urinary incontinence. But there are things you can do, like pelvic floor exercises, that can help you regain control of urine function.

Many side effects can be managed. Some can even be prevented. Ask your treatment team for a complete list of short- and long-term side effects and information on how to manage them.

Supportive care

Supportive care is for relieving the symptoms of cancer and the side effects of cancer treatment. It also helps with other issues related to cancer.

For more information on supportive care, see *Chapter 8: Supportive care and other assistance*.

Key points

- Treatment for bladder cancer depends on the stage and grade of your cancer, your overall health, and your preferences.
- Transurethral resection of bladder tumor (TURBT) is a procedure for examining tumors in the bladder wall and removing them.
- Radical cystectomy involves removing the bladder, nearby lymph nodes, and other organs in the pelvis.
- A urinary diversion is a surgical procedure done with a radical cystectomy. Its purpose is to provide a new way for urine to leave the body.
- Intravesical therapy is the use of cancer medicine placed directly into the bladder.
- Chemotherapy is treatment with drugs to kill cancer cells throughout the whole body. Most chemotherapy drugs are liquids that are slowly injected into a vein (infusion).
- All treatments for bladder cancer can cause side effects.

Questions to ask

- How will you know if the treatment is working? What are my options if the treatment stops working?
- Are my chances better for one treatment than another?
- If I have a radical cystectomy, what type of urinary diversion can I have?
- How do I get a second opinion?

What's your stage?

If you've reached this page, then you've probably been told the stage of your bladder cancer. Turn to the correct chapter to find out about your treatment.

If your urologist or another provider told you your cancer stage, but you don't remember or didn't understand, call the office and ask for more information. Someone there should be willing to explain it to you.

Turn to the chapter that matches your cancer stage to read about the types of treatment you may receive.



Take our survey and help make the NCCN Guidelines for Patients better for everyone!

NCCN.org/patients/comments

Your overall cancer stage	Chapter	Page
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0is	5. Non–muscle-invasive	41
1	5. Non–muscle-invasive	41
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5

Treatment for non–muscle-invasive bladder cancer

41 Stage 0 and stage 1 bladder cancer

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Treatment for non–muscle-invasive bladder cancer aims to reduce the chance of cancer coming back after treatment and to prevent the cancer from progressing to a more advanced stage.

Bladder cancer that hasn't grown into the muscle layer of the bladder wall is called non–muscle-invasive. Stage 0 and stage 1 bladder cancer are non–muscle-invasive.

Non–muscle-invasive bladder cancer can often be treated without removing the bladder.

Stage 0 and stage 1 bladder cancer

Stage 0 bladder cancer occurs only on the surface of the urothelial layer (inner lining) of the bladder. There are two types of stage 0 bladder cancer:

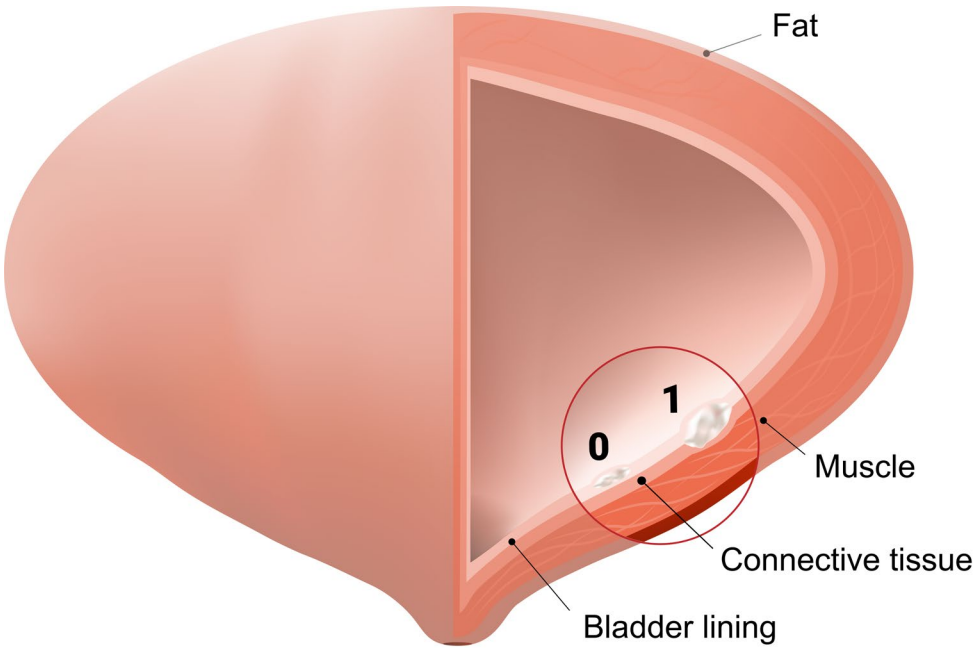
- **Stage 0a** (also called noninvasive papillary carcinoma) has finger-like projections that grow from the inner surface toward the hollow center of the bladder.
- **Stage 0is** (also called carcinoma in situ, or CIS) is a flat tumor on the inner lining of the bladder.

Stage 1 bladder cancer has grown into the layer of connective tissue of the bladder wall but hasn't reached the muscle layer.

Stage 0 and stage 1 bladder cancer

Stage 0 bladder cancer occurs only on the inner lining (urothelial layer) of the bladder wall.

Stage 1 bladder cancer has grown through the inner lining and into the layer of connective tissue, but it hasn't reached the muscle layer.



Treatment for stage 0 and stage 1 bladder cancer depends on whether the cancer has low, medium, or high risk of coming back (recurrence) or continuing to grow (progression).

The level of risk is based on certain features, including its stage, size, whether it's growing slow or fast (low or high grade), and whether there's more than one tumor. See **Guide 2** and **Guide 3**.

For example, a small, slow-growing stage 0a tumor has a low risk of recurrence or progression. On the other hand, cancer with multiple large, fast-growing stage 0a tumors has a high risk.

Your biopsy sample and your first transurethral resection of bladder tumor (TURBT) test typically reveal this risk.

A second (repeat) TURBT may be needed if the first TURBT didn't remove enough of the tumor or didn't remove any muscle tissue from the bladder wall. If the repeat TURBT finds that the cancer has invaded the muscle layer, the tumor will be treated as muscle-invasive bladder cancer (stage 2 or higher).

Also, you may have received a single dose of intravesical chemotherapy when you had your first TURBT. This can help prevent cancer recurrence. This one-shot intravesical treatment is separate from the 6-week course of intravesical therapy recommended in **Guide 2** and **Guide 3**.

Guide 2
Treatments for stage 0 and stage 1 low-risk or medium-risk bladder cancer

	Tumor characteristics		Treatment options
Low risk	• Small, single, slow-growing stage 0a lesion	→	• Surveillance
Medium risk	• Large slow-growing stage 0a tumor • Multiple slow-growing stage 0a tumors • Slow-growing stage 0a tumor that comes back 1 or more times within 1 year • Fast-growing stage 0a tumor • Slow-growing stage 1 tumor • Initial intravesical therapy didn't work	→	• Intravesical (BCG or chemo) therapy* • Surveillance

*Preferred treatment.

Treatment based on risk

You've had a lot of tests. Now your care team finally knows enough about your cancer to plan how to treat it.

Treatment for stage 0 and stage 1 cancers is based on the **risk** that the cancer will recur or progress.

Low-risk bladder cancer care doesn't include active therapy after you've had an initial TURBT. But it does involve surveillance.

Surveillance means occasional testing to see if the cancer reappears after it's been treated.

For stage 0 bladder cancer, surveillance involves a cystoscopy every 3 to 6 months after TURBT, and then once a year after that.

Medium-risk bladder cancer has a fair chance of recurring. Although surveillance is a reasonable option, the preferred treatment is a 6-week course of intravesical therapy of bacillus Calmette-Guérin (BCG) or chemotherapy.

Guide 3
Treatments for stage 0 and stage 1 high-risk bladder cancer

High-risk tumor characteristics	Did you have initial intravesical BCG therapy?	Recommended treatment options
• Large fast-growing stage 0a tumor • Multiple fast-growing stage 0a tumors	No →	• Initial intravesical BCG therapy, then maintenance BCG therapy • Intravesical chemotherapy • Clinical trial
	Yes, and it worked →	• Maintenance BCG therapy
• Fast-growing stage 0is tumor • Fast-growing stage 1 tumor	Yes, but it didn't work →	• Radical cystectomy • Clinical trial • Repeat initial intravesical BCG therapy • Intravesical chemotherapy (single or multiple drugs) • Other intravesical therapy

High-risk bladder cancer has a major risk of coming back or growing further. High-risk bladder cancer can be treated with intravesical BCG therapy if you haven't had BCG before or if the cancer didn't return until more than 2 years after your initial BCG therapy.

Other recommended options if you haven't had intravesical BCG therapy are intravesical chemotherapy or participating in a clinical trial.

If you have high-risk non–muscle-invasive bladder cancer but you can't have BCG therapy or if it doesn't work for you, then the preferred treatment options are either a radical cystectomy or a clinical trial.

If neither BCG therapy nor cystectomy can be done and a clinical trial isn't an option either, other recommended treatments are the gemcitabine intravesical system (Inlexzo) or standard intravesical chemotherapy with one or more chemotherapy drugs.

Additional treatment options are nadofaragene firadenovec (Adstiladrin) and nogapendekin alfa inbakicept (Anktiva). These are intravesical medicines that go directly into the bladder, where they boost the bladder's immune cells to fight cancer better.

High-risk bladder cancer with very high-risk feature(s) has a greater chance of progressing to an advanced stage, so radical cystectomy is the preferred treatment. However, a clinical trial or intravesical BCG might be an option in certain cases.

Very high-risk features include:

- Intravesical BCG therapy has no effect on the cancer.
- Tumor cells are found in the blood vessels or lymph vessels outside the main tumor (lymphovascular invasion).
- Cancer recurs (comes back) in the urethra.
- The cancer is a rare subtype that usually leads to poor outcomes.

Supportive care should also be available during treatment. Supportive care is for relieving cancer symptoms and treatment side effects.

Follow-up care

After treatment, the next phase of care will begin. This is the follow-up (or surveillance) phase. During this time, you'll have occasional tests to watch out for your cancer to return.

As mentioned elsewhere in this guide, bladder cancer often comes back at some point. So surveillance is always recommended after treatment ends.

People with bladder cancer need regular follow-up tests for many years to check if the cancer has returned. Make sure you go to all your follow-up appointments. (If you develop any symptoms or problems, don't wait until your next follow-up visit. Call your doctor or care team right away.)

The tests you should have—and how often you should have them—are guided by your risk of cancer recurrence. Each person's follow-up plan is different.

Depending on your type of cancer and other health considerations, you may need these follow-up tests:

- Cystoscopy
- Imaging of the upper urinary tract
- Imaging of the abdomen and pelvis
- Urine cytology
- Urinary tumor markers

If you didn't have your bladder removed as part of your treatment, see **Guide 4** for follow-up testing based on your risk level.

If your bladder was removed, see which follow-up tests you'll need in **Guide 5** on the next page.

Guide 4
Follow-up care by risk level for non–muscle-invasive bladder cancer

	Low risk	Medium risk	High risk
Cystoscopy	**Year 1:** At 3 and 12 months **Years 2-5:** Once a year **After that:** As directed by your doctor	**Year 1:** At 3, 6, and 12 months **Year 2:** Every 6 months **Years 3-5:** Once a year **After that:** As directed by your doctor	**Years 1-2:** Every 3 months **Years 3-5:** Every 6 months **Years 6-10:** Once a year **After that:** As directed by your doctor
Imaging of upper urinary tract, abdomen, and pelvis	**Year 1:** Baseline imaging with urogram (CT or MRI), pyelogram, or ureteroscopy **After that:** As directed by your doctor		**Year 1:** Baseline imaging, and again at 12 months **Years 2-10:** Every 1-2 years **After that:** As directed by your doctor
Urine cytology	None	**Year 1:** At 3, 6, and 12 months **Year 2:** Every 6 months **Years 3-5:** Once a year **After that:** As directed by your doctor	**Years 1-2:** Every 3 months **Years 3-5:** Every 6 months **Years 6-10:** Once a year **After that:** As directed by your doctor
Urine tumor marker testing	None		Your doctor may suggest this testing in the first 2 years after treatment.

Recurrence or progression

Follow-up care is all about watching for the recurrence of cancer. If cancer does return, it's helpful to know how to deal with it.

When cancer returns during follow-up therapy, it's usually detected by a cystoscopy exam. However, sometimes a urine cytology test indicates signs of cancer when cystoscopy doesn't.

Here's what will happen, depending on the results of these tests.

If cystoscopy finds cancer

If cancer appears on a follow-up cystoscopy test, you'll have another TURBT to re-assess the cancer risk. The level of risk indicates the appropriate treatment. See **Guide 2** and **Guide 3**.

For example, if you had medium-risk non–muscle-invasive bladder cancer and the repeat TURBT shows that the cancer has come back

Guide 5
Follow-up care after radical cystectomy for non–muscle-invasive bladder cancer

<table>
<tr><th></th><th>Imaging</th><th>Blood tests</th><th>Urine tests</th></tr>
<tr><td>Year 1</td><td>At 3 and 12 months:
• Urogram (CT or MRI) of upper urinary tract, abdomen, and pelvis</td><td>Every 3-6 months:
• Kidney function
• Liver function
• CBC and CMP (if you had chemotherapy)</td><td rowspan="2">Every 6-12 months:
• Urine cytology
• Urethral wash cytology (only if high risk of recurrence)</td></tr>
<tr><td>Year 2</td><td rowspan="3">Once a year:
• Urogram (CT or MRI) of upper urinary tract, abdomen, and pelvis</td><td rowspan="3">Once a year:
• Kidney function
• Liver function
• B12 level, if requested by your doctor</td></tr>
<tr><td>Year 3</td><td rowspan="3">As directed by your doctor:
• Urine cytology
• Urethral wash cytology (only if high risk of recurrence)</td></tr>
<tr><td>Year 4</td></tr>
<tr><td>Year 5</td><td rowspan="2">Once a year:
• Ultrasound of the kidneys</td><td rowspan="2">Once a year:
• B12 level, if requested by your doctor</td></tr>
<tr><td>Years 6-10</td></tr>
<tr><td>After 10 years</td><td>As directed by your doctor</td><td></td><td></td></tr>
</table>

as high-risk, you should begin treatment for high-risk cancer. After this treatment, you'll resume follow-up.

If urine cytology indicates cancer

If the results from a follow-up urine cytology test suggest cancer may have returned—and a second cytology test confirms the first one—then more testing is needed to pinpoint where the cancer is.

Further testing will look for cancer in the bladder as well as other areas, such as the prostate and upper urinary tract.

Tests may include:

- Biopsies of the urethra, bladder, or prostate
- Urine cytology of the upper urinary tract
- Ureteroscopy, a test that examines inside of the kidneys and ureters

If the biopsy of the bladder finds cancer, you'll have another TURBT to find out your current level of risk. See **Guide 2** and **Guide 3**.

Treatment for other test results:

- If none of the tests detect cancer, you should have a follow-up visit in 3 months to confirm it.
- If a biopsy finds cancer in the prostate, then further testing and treatment of the prostate are needed.
- If a urine cytology of the upper tract indicates cancer, then you'll need further testing and treatment of the upper urinary tract.

After treatment, your follow-up schedule will depend on the current stage of your cancer and what treatment you've already received.

What's next?

You'll continue to have tests and follow-up visits every so often to watch out for the cancer to return or progress. Surveillance is a key part of the follow-up plan.

There are many new and exciting treatments for bladder cancer recently approved and on the horizon. As always, you can try to join a clinical trial at almost any point during cancer care.

Consider joining a support group. Talking with other people who have bladder cancer can be informative and reassuring.

Know that you can have bladder cancer and still lead a fulfilling life after diagnosis and treatment.

Key points

- Non–muscle-invasive cancer is often treated without removing the bladder.
- Surveillance is often the best care for low-risk non–muscle-invasive bladder cancer. Surveillance means occasional testing to find out if cancer has returned.
- The preferred treatment for medium-risk non–muscle-invasive bladder cancer is intravesical therapy with either bacillus Calmette-Guérin (BCG) or chemotherapy.
- High-risk non–muscle-invasive bladder cancer may be treated with a radical cystectomy or perhaps a clinical trial. Intravesical BCG therapy might be an option in certain cases.
- Follow-up testing is based on the risk of the cancer returning. The higher your risk, the more tests you'll need.

Questions to ask

- Where will I receive treatment—in a hospital, a clinic, your office, or at home?
- How long will the treatment last?
- Will the treatment hurt?
- What are the chances of the cancer worsening or returning?
- What follow-up care is needed after my treatment?

6

Treatment for muscle-invasive bladder cancer

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64 Questions to ask

Muscle-invasive bladder cancer means that the tumor has grown deep enough to reach the thick layer of muscle in the bladder wall. This is often treated with surgery to remove the bladder or with chemoradiation therapy.

This chapter covers treatment for cancer that has grown into the muscle layer of the bladder wall. This includes stages 2 to 4A.

If you know your cancer stage, turn to the page that describes the treatment for that stage.

Stage 2 and stage 3A bladder cancer

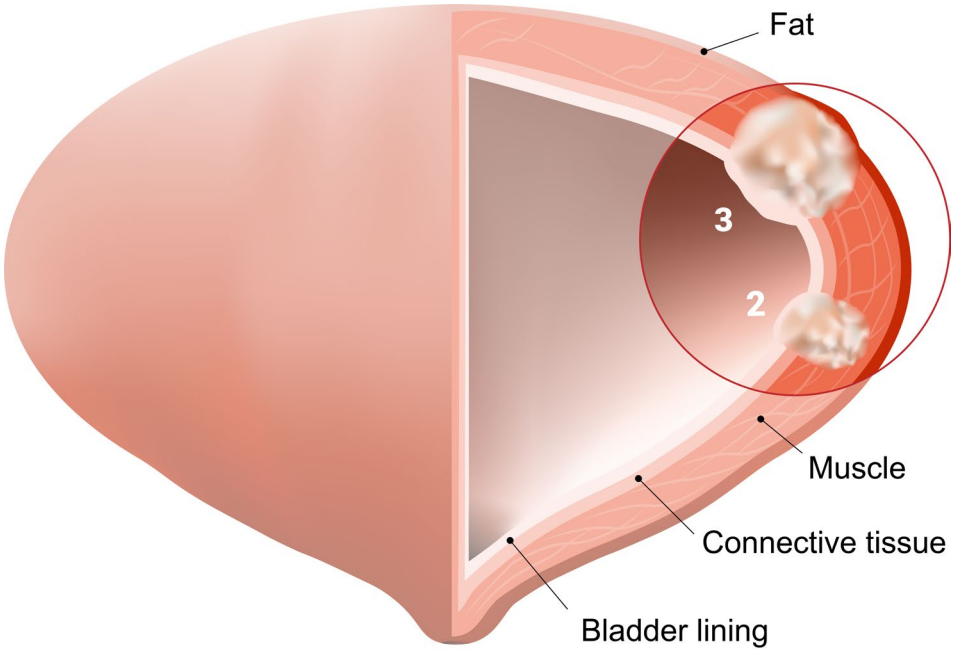
Stage 2 bladder cancer has grown into the muscle layer, but it hasn't reached the fatty tissue covering the bladder, nor has it spread anywhere else. Stage 2 bladder cancer is likely to have a better outcome than cancer that has reached the fatty layer or beyond.

Stage 3A bladder cancer has grown through the bladder wall to the fatty layer surrounding the bladder. It may have spread to nearby reproductive organs, such as the prostate gland, seminal vesicles, uterus, or vagina. Or it may have spread to a nearby lymph node. Stage 3A cancer has not spread to the walls of the pelvis or the abdomen, or to nodes or organs far from the bladder.

Stage 2 and stage 3A bladder cancer

Stage 2 bladder cancer has grown into the muscle layer but it hasn't reached the fatty outer layer or spread anywhere else.

Stage 3A bladder cancer has grown through the bladder wall to the fatty layer. It may also have spread to nearby reproductive organs or a nearby lymph node.



The main treatment for stage 2 and stage 3A bladder cancer is a radical cystectomy. This is a surgery that removes the cancer by taking out the entire bladder and nearby lymph nodes. Also, the prostate is removed in males and the uterus, cervix, fallopian tubes, ovaries, and part of the vagina may be removed in females.

Combination chemotherapy with cisplatin is often given before a cystectomy to shrink the tumor prior to the surgery and to kill any cancer cells that might be outside the bladder.

Another method now being used consists of a combination of chemotherapy and immunotherapy given before the radical cystectomy and then additional immunotherapy given after the surgery.

To choose the best treatment for your needs, you and your treatment team will consider these two important questions:

- Can you tolerate chemotherapy with the drug cisplatin?
- Are you healthy enough to have major surgery to remove your bladder?

To help answer these questions, you'll receive further evaluation, such as CT or MRI imaging of the abdomen and pelvis. Another essential test checks the health of your kidneys. This is a simple blood test to make sure your kidneys are working well enough to handle the stress that chemotherapy will put on them.

Some people with stage 2 bladder cancer can't have surgery or don't want it. If this describes you, skip the next section and go to "Treatment without bladder removal" on page 53.

If you do expect to have a radical cystectomy, read the following section.

Bladder removal surgery

Radical cystectomy can be done with or without chemotherapy. It depends on whether you're able to have chemotherapy. If you can, you might also be able to add immunotherapy to this treatment.

For recommended treatment options, see **Guide 6**.

Guide 6
Stages 2 and 3A initial treatment options for radical cystectomy

- Radical cystectomy and chemotherapy
- Radical cystectomy with a combination of chemotherapy and immunotherapy
- Radical cystectomy with a combination of targeted therapy and immunotherapy
- Radical cystectomy alone

Each procedure also involves a urinary diversion.

Radical cystectomy and chemotherapy

This option starts with a combination of chemotherapy drugs, one of which is cisplatin. Cisplatin has been shown to be the most effective type of chemotherapy for treating bladder cancer.

About 1 to 2 months after finishing chemotherapy, you'll have surgery to remove the bladder (radical cystectomy). A radical cystectomy is often the best option to treat muscle-invasive bladder cancer and help prevent it from returning. During the radical cystectomy procedure, the surgeon will also create a urinary diversion.

Radical cystectomy with a combination of chemotherapy and immunotherapy

This newer treatment approach combines the most effective chemotherapy—cisplatin—with immunotherapy to improve outcomes. This approach can further delay cancer from coming back and appears to help people live longer.

The treatment process is almost the same as standard chemotherapy and radical cystectomy. But this treatment adds the immunotherapy drug durvalumab (Imfinzi) to the cycles of chemotherapy before the radical cystectomy. After surgery, patients will receive several additional cycles of durvalumab immunotherapy.

Some doctors call this a "sandwich" treatment because the 2 courses of immunotherapy occur with surgery in the middle, like slices of bread in a sandwich.

Radical cystectomy with a combination of targeted chemotherapy and immunotherapy

This is also a sandwich treatment. But for this treatment, the targeted chemotherapy/antibody-drug conjugate drug enfortumab vedotin (Padcev) is combined with the immunotherapy pembrolizumab (Keytruda) for a few cycles before a radical cystectomy.

After the cystectomy, treatment is several cycles of enfortumab vedotin combined with a dozen or so cycles of pembrolizumab.

Radical cystectomy alone

This is another option for people who can't have cisplatin-based chemotherapy. Cisplatin may be too harsh for some people, especially those whose liver and kidneys don't work well.

If you have hearing loss, nerve damage, or are unable to do most daily activities, then you also may not be able to have cisplatin-based chemotherapy.

In such cases, radical cystectomy is the most appropriate option.

Treatment after bladder surgery

Depending on what the surgeon sees firsthand during the radical cystectomy and whether certain findings are on your pathology report, you may have additional therapy to get rid of any cancer cells that remain after the surgery.

Reasons why you may need additional treatment:

- The tumor is larger than expected.
- The tumor has grown through the bladder wall.
- Cancer has reached the lymph nodes.

The choice of additional treatment is based in part on whether you received therapy before surgery. See **Guide 7**.

Follow-up

For recommendations on follow-up care and monitoring for cancer recurrence, see “Follow-up care” on page 60.

Treatment without bladder removal

Not everyone may need, want, or be able to have a radical cystectomy. If you have other serious health problems or you’re physically unable to do many day-to-day activities, surgery may not be a good option for you. Or your tumor may be small enough to be removed without removing the whole bladder.

Bladder cancer treatment that doesn’t involve radical cystectomy is called bladder-preserving treatment. Bladder-preserving treatment options include trimodal therapy or radiation therapy alone.

Trimodal therapy

Trimodal therapy is a bladder-preserving treatment for certain people with muscle-invasive bladder cancer.

In trimodal therapy, TURBT (transurethral resection of bladder tumor) first removes any visible tumor, and then chemotherapy and radiation are used together to kill any cancer cells left over. Trimodal therapy may be a good option if **Guide 8** describes your cancer.

Radiation therapy alone

If you’re not able to have chemoradiation and you’re not able or don’t want to have a radical cystectomy, radiation therapy alone is a possible treatment option for people with stage 2 or stage 3A bladder cancer.

What’s next?

After you’ve finished your initial treatment, your bladder should be re-examined with a CT scan and possibly a cystoscopy. Depending on whether cancer is still found, this is generally what might happen next:

If no cancer is found, you can begin follow-up care and monitoring without further treatment.

If cancer is still there and you can have a radical cystectomy, further treatment is based on the type and size of the remaining tumor. Options include TURBT with or without intravesical therapy if the tumor is now stage 1,

Guide 7
Stages 2 and 3A additional treatment after radical cystectomy

Additional treatment options	Requirements
Cisplatin-based chemotherapy (preferred)	• You didn't have chemotherapy before surgery, **and** • The cancer was stage 3 or higher or had spread to lymph nodes at the time of surgery.
Immunotherapy with Durvalumab (Imfinzi)	• You had cisplatin-based chemotherapy and durvalumab before surgery.
Targeted chemotherapy with Enfortumab vedotin (Padcev) and immunotherapy with Pembrolizumab (Keytruda)	• You had enfortumab vedotin combined with pembrolizumab before surgery.
Immunotherapy with Nivolumab (Opdivo) or Pembrolizumab	• You had cisplatin-based chemotherapy before surgery, and the cancer was stage 2 or higher or had spread to lymph nodes at the time of surgery, **or** • You didn't have chemotherapy before surgery, and the cancer was stage 3 or higher or had spread to lymph nodes at the time of surgery.
Immunotherapy with Atezolizumab (Tecentriq)	• You still have a small amount of cancer cells in your body (as determined by a specific DNA test), **and** • You had bladder surgery less than 1 year ago.
Radiation therapy (in certain cases)	• The cancer was stage 3 or higher and/or had spread to lymph nodes at the time of surgery.

a radical cystectomy (or a partial cystectomy in very specific cases) if the tumor is stage 2, or treatment for metastatic cancer.

If cancer is still there but you can't have or don't want a radical cystectomy, further treatment is based on the type and size of the remaining tumor. If the tumor is now stage 1, further treatment is TURBT with or without intravesical therapy. If the tumor has grown beyond stage 1, treatment for metastatic cancer is given. Supportive care is recommended no matter what treatment you have.

Follow-up

For recommendations about follow-up care and monitoring for the return of cancer, see "Follow-up care" on page 60.

Stage 3B bladder cancer

Stage 3B bladder cancer is considered locally advanced. This means the cancer has grown outside the bladder and spread to multiple lymph nodes in the pelvis or to at least one lymph node in the upper pelvic region. But the cancer has not spread to organs or lymph nodes far from the bladder. (So this stage is not metastatic.)

Systemic therapy

The main treatment for stage 3B bladder cancer is systemic therapy. Systemic therapy affects the whole body, not just part of it. The goal of systemic therapy is to shrink the tumor as much as possible and, most importantly, kill any cancer cells outside the bladder.

Guide 8
Can you have bladder-preserving treatment?

Chemoradiation without radical cystectomy is an option only for some people with muscle-invasive bladder cancer. Every person is different, but here are some **common characteristics** of people who can have bladder-preserving treatment.

- The tumor is smaller than 6 centimeters (about as long as an egg).
- The tumor is not blocking the flow of urine from the kidneys into the bladder.
- There's no carcinoma in situ (CIS). CIS is an area of flat, fast-growing cancer cells on the inside lining of the bladder.
- The tumor can be entirely removed by TURBT.

The most common systemic therapies for locally advanced bladder cancer are chemotherapy, targeted therapy, and immunotherapy. The recommended treatment options are listed in **Guide 9**.

Additional treatment may be needed, depending on how well the main therapy works.

The standard treatment for locally advanced bladder cancer has long been platinum-based chemotherapy (cisplatin or carboplatin).

More recently, cancer experts have begun treating locally advanced and metastatic bladder cancer with a combination of a targeted therapy (enfortumab vedotin, an antibody-drug conjugate named Padcev) and an immunotherapy (pembrolizumab, Keytruda).

This combination appears to be more effective than platinum-based chemotherapy for stage 3B cancer.

If you're not able to have this combination treatment, platinum-based chemotherapy and other immunotherapy and targeted therapy medicines are still recommended treatment options.

Guide 9
Initial systemic therapy for stage 3B and stage 4A bladder cancer

	Treatment	Maintenance therapy
Preferred option	Enfortumab vedotin (Padcev) and Pembrolizumab (Keytruda)	
Other recommended therapies	Cisplatin and Gemcitabine	Avelumab (Bavencio)
	Gemcitabine, Cisplatin, and Nivolumab (Opdivo)	Avelumab
	Dose-Dense Methotrexate, Vinblastine, Doxorubicin, and Cisplatin (ddMVAC)	Avelumab
Therapies used in certain cases	Gemcitabine and Carboplatin	Avelumab
	Pembrolizumab	
	Atezolizumab (Tecentriq)	

Additional therapy

After you've finished your initial therapy, you'll have imaging tests to see if the treatment worked.

If no cancer is found or if there's less cancer after initial treatment, your next step depends on your specific circumstances:

- Monitoring without additional treatment. This doesn't necessarily mean the cancer has been cured. So you'll begin follow-up visits to watch for the cancer to return.
- Having additional therapy to wipe out any undetectable cancer cells that may be left behind. Treatment options include:
  - Radical cystectomy
  - Chemoradiation therapy
- Continuing with the systemic therapy you had as your initial treatment.

If the cancer continues to grow or spread despite initial therapy, then the next step is to begin treatment for metastatic disease. See *Chapter 7: Treatment for metastatic bladder cancer*.

Follow-up

For recommendations on follow-up care and monitoring for the return of cancer, see "Follow-up care" on page 60.

Stage 4A bladder cancer

Stage 4A bladder cancer has grown through the bladder wall and may have spread to the wall of the pelvis or the wall of the abdomen. Stage 4A may have spread to lymph nodes near the bladder and even to lymph nodes far from the bladder.

Treatment options for stage 4A bladder cancer depend on whether the cancer has or hasn't spread to far away lymph nodes.

Stage 4A bladder cancer that **has** spread to distant lymph nodes is considered metastatic. (See "Stage 4A metastatic" on the next page.)

Surveillance is a key part of your follow-up plan. Be sure to go to follow-up visits and stay in touch with your treatment team.



Stage 4A cancer that **hasn't** reached distant lymph nodes is called locally advanced.

Stage 4A locally advanced

If tests show that cancer has spread to the wall of the pelvis or abdomen but has not spread to distant lymph nodes or organs, your initial therapy may be systemic therapy.

Systemic therapy combines a targeted chemotherapy (enfortumab vedotin, Padcev) and an immunotherapy (pembrolizumab, Keytruda). This combination is usually more effective than platinum-based chemotherapy for this stage of cancer. See **Guide 9**.

If you're not able to have this combination therapy, you can have platinum-based chemotherapy and/or a different immunotherapy medicine.

Additional therapy

After treatment, you'll need a few tests to see if the therapy worked.

If no cancer is found after initial therapy, additional treatment may prevent the cancer from coming back. Options include:

- Continue with the systemic therapy you had as your initial treatment.
- Radiation therapy (if you haven't had radiation therapy before).
- Radical cystectomy (if the main treatment shrank the tumor enough).

If cancer is found after initial treatment, you may choose to have further treatment to continue to shrink the cancer. Additional treatment options include:

- Systemic therapy, such as chemotherapy, immunotherapy, and/or targeted therapy. For further systemic therapy options, see **Guide 10**.
- Chemoradiation therapy (if you haven't had radiation therapy before).
- Radical cystectomy (if the main treatment shrank the tumor enough).

You can also consider participating in an appropriate clinical trial.

Follow-up

For recommendations on follow-up care and monitoring for cancer recurrence, see "Follow-up care" on page 60.

Stage 4A metastatic

Stage 4A cancer has spread to distant lymph nodes in the body (metastasized) but hasn't grown or spread to distant organs. The main treatment is systemic therapy, which is treatment that affects cancer cells throughout the body.

For recommended systemic therapy options, see **Guide 9**.

If you had platinum-based chemotherapy as your initial treatment and your cancer doesn't grow or spread as a result, then you may have maintenance therapy after initial treatment to retain the benefits of the chemotherapy and to slow the cancer from growing.

Guide 10
Next systemic therapy options for stage 4A bladder cancer

What was your initial therapy?	Preferred next therapy options	Other recommended next therapy options
Immunotherapy and targeted chemotherapy (Enfortumab vedotin, Padcev)	• Biomarker-targeted therapy: – Erdafitinib (Balversa) – Trastuzumab deruxtecan (Enhertu) • Cisplatin and Gemcitabine • Dose-Dense Methotrexate, Vinblastine, Doxorubicin, and Cisplatin (ddMVAC) • Carboplatin and Gemcitabine	• Gemcitabine • Paclitaxel (Taxol) or Docetaxel
Chemotherapy	• Enfortumab vedotin and Pembrolizumab (Keytruda)	• Pembrolizumab • Biomarker-targeted therapy: – Erdafitinib – Trastuzumab deruxtecan • Enfortumab vedotin • Avelumab (Bavencio) • Nivolumab (Opdivo)
Immunotherapy	• Biomarker-targeted therapy: – Erdafitinib – Trastuzumab deruxtecan • Carboplatin and Gemcitabine • Cisplatin and Gemcitabine • ddMVAC • Enfortumab vedotin • Enfortumab vedotin and Pembrolizumab	• Gemcitabine • Paclitaxel or Docetaxel
Chemotherapy and immunotherapy	• Enfortumab vedotin • Biomarker-targeted therapy: – Erdafitinib – Trastuzumab deruxtecan	• Cisplatin and Gemcitabine • ddMVAC • Enfortumab vedotin and Pembrolizumab • Gemcitabine • Paclitaxel or Docetaxel • Doxorubicin, Gemcitabine, and Ifosfamide • Gemcitabine and Paclitaxel

Maintenance therapy involves one of the immunotherapy checkpoint inhibitors avelumab (Bavencio) or nivolumab (Opdivo).

Additional therapy

After initial treatment, you'll have a few tests to see if the therapy worked.

If no cancer is found or there's less cancer after initial therapy, then your doctor may ask you to consider surgery or radiation to get rid of any cancer in the bladder that may be left behind. This treatment is mostly for people who want to be very aggressive with therapy and had good results with systemic therapy.

If the cancer stays the same or continues to grow, your next step is treatment for metastatic disease. See *Chapter 7: Treatment for metastatic bladder cancer*.

You can also consider joining a clinical trial.

Follow-up care

When you've finished initial treatment and any additional treatment, the next phase of cancer care will begin. This is the follow-up (or surveillance) phase. During this time, you'll have occasional tests to watch out for your cancer to return.

As mentioned elsewhere in this guide, bladder cancer can come back at any time. So be sure not to skip or forget any follow-up appointments.

If you have any symptoms or problems, don't wait until your next follow-up visit. Call your doctor or care team right away.

The specific tests you should have—and how often you should have them—depend on whether your bladder was or wasn't removed.

If your bladder was removed

Even if you've had surgery to remove your bladder, cancer can come back in other areas, such as the upper urinary tract, the urethra, or elsewhere in your body. So you can expect to have follow-up tests and visits for many years.

Follow-up after a radical cystectomy includes imaging, urine and blood tests, and tests to check your liver and kidney health. For the recommended schedule of follow-up testing after a radical cystectomy, see **Guide 11**.

Keep in mind that every person's follow-up plan is different.

Urethral wash cytology is a test that looks for cancer in the urethra. For this test, the urethra is filled with a salt solution. The fluid is then flushed out and tested for cancer cells. Urethral wash cytology is usually only done when there's a high risk of cancer recurrence in the urethra.

People who've had a urinary diversion may develop a loss of vitamin B12 over time. So their vitamin B12 level should be checked once per year after the first year of follow-up care.

If your bladder wasn't removed

If you didn't have a radical cystectomy, there's always a risk that cancer will return to the bladder, another part of the urinary tract, or other areas of the body.

Follow-up tests after bladder-preserving treatment include cystoscopy, imaging, urine and blood tests, and tests to check your liver and kidney health.

For the recommended schedule of follow-up testing after bladder-preserving treatment, see **Guide 12**.

Keep in mind that every person's follow-up plan will be different.

Guide 11
Follow-up tests after radical cystectomy for muscle-invasive bladder cancer

<table>
<tr><th></th><th>Imaging</th><th>Blood tests</th><th>Urine tests</th></tr>
<tr><td>Year 1</td><td rowspan="2">Every 3-6 months:
• Urogram (CT or MRI)
• Chest CT or chest x-ray
• PET/CT (only if metastasis is suspected)</td><td>Every 3-6 months:
• Kidney function
• Liver function
• CBC and CMP (if you had chemotherapy)</td><td rowspan="2">Every 6-12 months:
• Urine cytology
• Urethral wash cytology (only if high risk of recurrence)</td></tr>
<tr><td>Year 2</td><td rowspan="3">Once a year:
• Kidney function
• Liver function
• B12 level (only if your doctor recommends it)</td></tr>
<tr><td>Year 3</td><td rowspan="3">Once a year:
• CT or MRI of abdomen and pelvis
• Chest CT or chest x-ray
• PET/CT (only if metastasis is suspected)</td><td rowspan="3">As directed by your doctor:
• Urine cytology
• Urethral wash cytology (only if high risk of recurrence)</td></tr>
<tr><td>Year 4</td></tr>
<tr><td>Year 5</td></tr>
<tr><td>Years 6-10</td><td>Once a year:
• Ultrasound of the kidneys</td><td rowspan="2">Once a year:
• B12 level (only if your doctor recommends it)</td></tr>
<tr><td>After 10 years</td><td>As directed by your doctor</td></tr>
</table>

Recurrence or persistence

Bladder cancer comes back more often than almost any other type of cancer. Even people who received the most thorough treatment for bladder cancer can have recurrence.

Follow-up care is all about carefully watching for recurrence. When cancer returns, or when treatment doesn't get rid of it (persistence), it's helpful to know how to deal with it.

Treatment for recurrent or persistent muscle-invasive bladder cancer is based on the results of follow-up tests and whether your bladder was or wasn't removed.

Guide 12
Follow-up tests after bladder-preserving treatment for muscle-invasive bladder cancer

<table>
<tr><th></th><th>Cystoscopy</th><th>Imaging</th><th>Blood tests</th><th>Urine tests</th></tr>
<tr><td>Year 1</td><td rowspan="2">Every 3 months</td><td rowspan="2">Every 3-6 months:
• Urogram (CT or MRI)
• Chest CT or chest x-ray
• FDG-PET/CT (only if metastasis is suspected)</td><td>Every 3-6 months:
• Kidney function
• Liver function
• CBC and CMP (if you had chemotherapy)</td><td rowspan="2">Every 6-12 months:
• Urine cytology</td></tr>
<tr><td>Year 2</td><td rowspan="5">As directed by your doctor:
• Kidney function
• Liver function</td></tr>
<tr><td>Year 3</td><td rowspan="2">Every 6 months</td><td rowspan="2">Once a year:
• CT or MRI of abdomen and pelvis
• Chest CT or chest x-ray
• FDG-PET/CT (only if metastasis is suspected)</td><td rowspan="3">As directed by your doctor:
• Urine cytology</td></tr>
<tr><td>Year 4</td></tr>
<tr><td>Year 5</td><td rowspan="2">Once a year</td></tr>
<tr><td>Years 6-10</td><td rowspan="2">As directed by your doctor</td></tr>
<tr><td>After 10 years</td><td>As directed by your doctor</td></tr>
</table>

If your bladder was removed

If your bladder was removed but cancer has recurred, you'll have more tests to locate exactly where the cancer is.

Treatment for recurrent cancer if your bladder was removed may include systemic therapy, such as chemotherapy, immunotherapy, targeted therapy, and/or radiation therapy for pain relief.

If your bladder wasn't removed

If cancer is found in a person whose bladder wasn't removed, it's important to know whether the cancer is in the bladder or in another part of the urinary tract.

Cancer in the bladder

If tests show cancer has returned in the bladder but is not found in other areas of the body, treatment depends on whether cancer has invaded the bladder's muscle layer.

- **Not invaded the muscle layer** – These tumors are usually treated with intravesical bacillus Calmette-Guérin (BCG) therapy, transurethral resection of bladder tumor (TURBT), or a radical cystectomy.
- **Invaded the muscle layer** – These tumors are usually treated with a radical cystectomy. Chemoradiation is also an option if you haven't had radiation therapy before. If you can't have cystectomy or chemoradiation, other options are systemic therapy, such as immunotherapy or chemotherapy, as well as TURBT and palliative care for relief of pain and other symptoms.

Cancer in another part of the urinary tract

If urine cytology testing indicates cancer somewhere in the urinary tract, the next step is to find out where the cancer is located.

Additional tests are used to check the upper urinary tract and the urethra. These cancers are rare, but they can be very serious.

- **Cancer in the ureters or kidneys** – To check the upper urinary tract, you may have additional urine cytology tests and possibly biopsies of the ureters or kidneys. If cancer cells are found, treatment of the upper urinary tract is needed.
- **Cancer in the prostatic urethra** – A biopsy is done to check the section of urethra that runs through the prostate gland. If the biopsy shows cancer cells, treatment is needed for this part of the urethra.

What's next?

If you've been treated for recurrent or persistent cancer, you'll continue to have tests and follow-up visits to watch for the cancer to return or progress. Be sure to continue to go to follow-up visits and stay in touch with your treatment team. Surveillance is a key part of the follow-up plan.

Keep in mind that there are many new and exciting treatments for bladder cancer recently approved and on the horizon. As always, you can try to join a clinical trial at almost any point during cancer care.

Know that you can have bladder cancer and still lead a fulfilling life after diagnosis and treatment.

Ask about supportive care, which can be helpful at any stage of cancer. For information, turn to *Chapter 8: Supportive care and other assistance*.

Key points

- If a bladder tumor grows into the thick layer of muscle in the bladder wall, it's called muscle-invasive bladder cancer. Stage 2, 3, and 4 bladder cancer are muscle invasive.
- Radical cystectomy is the main treatment for people with stage 2 or 3A bladder cancer who are healthy enough for surgery. Chemotherapy is often given before surgery to shrink the tumor. Immunotherapy both before and after surgery is sometimes added to chemotherapy.
- When a radical cystectomy can't be done or isn't wanted, treatment options include transurethral resection of bladder tumor (TURBT) and chemoradiation, or radiation therapy alone.
- The main treatment for stage 3B and 4A bladder cancer is systemic therapy. Additional treatment is also sometimes needed.
- Follow-up testing after treatment for muscle-invasive bladder cancer includes imaging, urine and blood tests, and tests to check your liver and kidney health.

Questions to ask

- Does this hospital/center offer the best treatment for me?
- How do my age, sex, overall health, and other factors affect my options?
- How will you know if the treatment is working? What are my options if the treatment stops working?
- Are you suggesting treatment options from the NCCN Guidelines, or have you modified the standard treatment in my situation?
- If I have radical cystectomy with a urinary diversion, what can be done to preserve my urinary and sexual function?

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Treatment for metastatic bladder cancer

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72 Key points

72 Questions to ask

If cancer spreads to areas outside the bladder, it's called stage 4B or metastatic cancer. Treatment of metastatic bladder cancer is focused on helping you live as normally and as comfortably as possible, for as long as possible.

Stage 4B bladder cancer

Stage 4B is metastatic bladder cancer. This cancer has grown through the bladder wall and has spread (metastasized) to lymph nodes or areas like the bones, liver, or lungs.

Although treatments are improving all the time, metastatic bladder cancer is frequently incurable, and symptoms are common. For this reason, treatment is aimed at relieving symptoms while also slowing the growth and spread of cancer. Joining a clinical trial is also a good option for people who have metastatic bladder cancer.

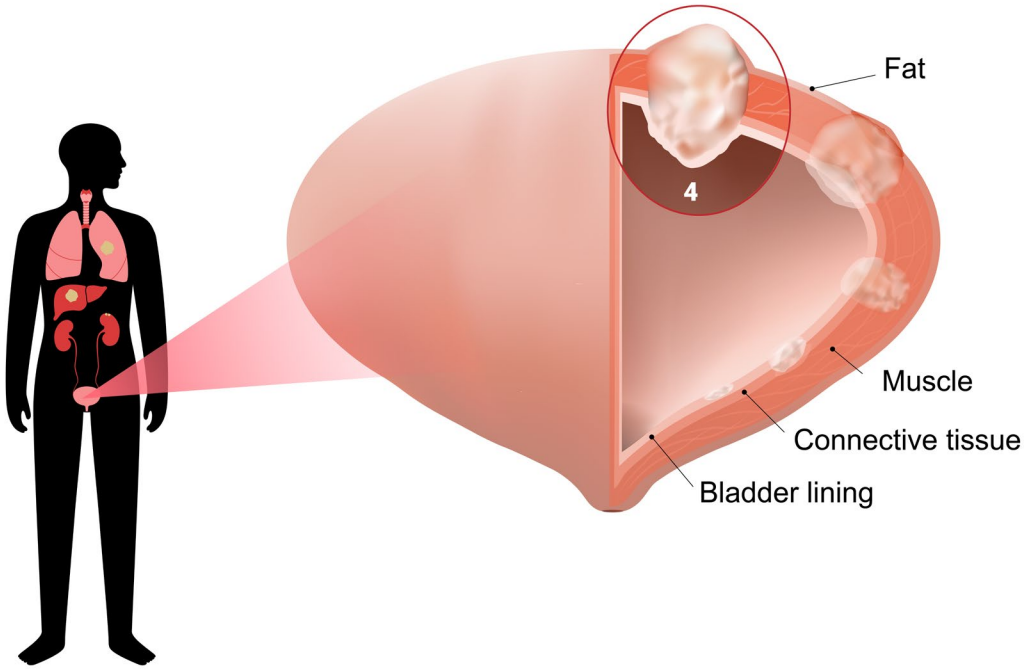
Being diagnosed with metastatic bladder cancer is very difficult. It can cause a lot of anxiety and stress. Talking about it with doctors, nurses, therapists, or counselors, as well as other people with bladder cancer, can be helpful. Ask your treatment team about available resources and see page 80 for a list of other resources.

Tests to plan treatment

Before treatment, you'll need more tests to find out how many metastases there are and where they are in your body. This information helps your treatment team plan the right care for you.

Stage 4B bladder cancer

Stage 4B bladder cancer has grown through the bladder wall and has spread (metastasized) to lymph nodes or organs far from the bladder.



The main treatment for metastatic bladder cancer is usually systemic therapy. Systemic therapies—like chemotherapy, immunotherapy, and targeted therapy—affect the whole body.

To determine which systemic therapy medicine is best for you, your care team will consider your overall health. This includes how your heart, liver, and kidneys are functioning, how far the cancer has progressed, and how well your body can tolerate intense treatment.

Tests may include:

- Bone scan or MRI to look for any cancer in your bones
- CT of your chest to look for cancer in your lungs and other organs
- CT or MRI imaging of your brain and spinal cord
- Blood test to see if your kidneys can process chemotherapy drugs
- Biopsy of any suspicious areas
- Biomarker testing to confirm that you can have certain targeted therapies

First-line therapy

NCCN experts recommend starting with one of the systemic therapy options in **Guide 13**. These are called first-line therapies because they have the best chance of working, so they should be used first.

Guide 13
Initial systemic therapy for stage 4B bladder cancer

	Treatment	Maintenance therapy
Preferred therapy	Enfortumab vedotin (Padcev) and Pembrolizumab (Keytruda)	
Other recommended therapies	Cisplatin and Gemcitabine	Avelumab (Bavencio)
	Cisplatin, Gemcitabine, and Nivolumab (Opdivo)	Avelumab
	Dose-Dense Methotrexate, Vinblastine, Doxorubicin, and Cisplatin (ddMVAC)	Avelumab
Therapies used in certain cases	Carboplatin and Gemcitabine	Avelumab
	Pembrolizumab	
	Atezolizumab (Tecentriq)	

The standard first-line treatment for metastatic bladder cancer has long been platinum-based chemotherapy (cisplatin or carboplatin). But cancer experts are now treating metastatic bladder cancer with a combination of a targeted chemotherapy (enfortumab vedotin, Padcev) and an immunotherapy (pembrolizumab, Keytruda). This combination appears to be more effective than platinum-based chemotherapy for metastatic bladder cancer.

If you're not able to have this combination treatment or if it's unavailable, platinum-based chemotherapy and other immunotherapy and targeted therapy medicines are still recommended for treating metastatic bladder cancer.

Maintenance therapy

If you had platinum-based chemotherapy as your first-line therapy and your cancer hasn't grown or spread, then you may have maintenance therapy to retain the benefits of first-line chemotherapy and to slow the cancer from growing.

Maintenance therapy usually involves the checkpoint inhibitor avelumab (Bavencio) or sometimes nivolumab (Opdivo).

Maintenance therapy is not usually required after other types of first-line systemic therapy.

Radiation for symptom relief

For some people with metastatic bladder cancer, radiation therapy can be used to reduce symptoms and to ease pain or discomfort in your bones or elsewhere.

"Be your own advocate. Ask a lot of questions, even the ones you are afraid to ask. Don't be afraid to ask for a second opinion. You have to protect yourself and ensure you make the best decisions for you, and get the best care for your particular situation."

Because this type of radiation doesn't aim to cure the cancer, lower doses can be used. This lessens the side effects commonly associated with radiation therapy. Ask your treatment team if you're able to have this kind of radiation treatment.

Clinical trials

Joining a clinical trial is an option for anyone with cancer. It's especially recommended for people whose bladder cancer continues to advance after first-line treatment.

Follow-up

After you've been on therapy for a while, your treatment team will want to see how well the therapy is working. Follow-up tests are listed in **Guide 14**.

If the cancer stays the same or improves, you'll likely continue to have the same treatment.

If the cancer continues to grow (progresses) or if the treatment is too harsh, a different treatment should be considered.

Next treatment options

If cancer progresses after first-line therapy, there are other treatments you can have next. Recommended next treatment options are shown in **Guide 15**. These options depend on which first-line therapy you had.

If you had chemotherapy as first-line treatment, then the preferred next treatment options are pembrolizumab, enfortumab vedotin, enfortumab vedotin and pembrolizumab together, nivolumab, or avelumab.

If testing shows your cancer has a certain biomarker, then you might have erdafitinib (Balversa) if it's a change in the *FGFR3* gene or trastuzumab deruxtecan (Enhertu) if it makes too much HER2 protein.

If your first-line treatment was immunotherapy, such as pembrolizumab, nivolumab, or atezolizumab (Tecentriq), then the preferred next treatment options include enfortumab vedotin, or enfortumab vedotin and pembrolizumab together.

Preferred chemotherapy options include combinations of gemcitabine and carboplatin, gemcitabine and cisplatin, or methotrexate, vinblastine, doxorubicin, and cisplatin (ddMVAC).

Guide 14
Follow-up tests after first-line treatment for stage 4B bladder cancer

Test	Test frequency
Cystoscopy	**As directed by your doctor**
Imaging	**Every 3-6 months, or sooner if there's any change or new symptoms:** • Urogram (CT or MRI) • CT or PET/CT scan of chest, abdomen, and pelvis • PET/CT
Blood tests	**Every 1-3 months:** • Complete blood count (CBC), comprehensive metabolic panel (CMP) **Once a year:** • B12 level if you had a cystectomy and if requested by your doctor
Urine tests	**As directed by your doctor:** • Urine cytology

Guide 15
Next systemic therapy options for stage 4B metastatic bladder cancer

What was your initial therapy?	Preferred next therapy options	Other recommended next therapy options
Immunotherapy and targeted chemotherapy (Enfortumab vedotin, Padcev)	• Biomarker-targeted therapy: – Erdafitinib (Balversa) – Trastuzumab deruxtecan (Enhertu) • Cisplatin and Gemcitabine • Dose-Dense Methotrexate, Vinblastine, Doxorubicin, and Cisplatin (ddMVAC) • Carboplatin and Gemcitabine	• Gemcitabine • Paclitaxel (Taxol) or Docetaxel
Chemotherapy	• Enfortumab vedotin and Pembrolizumab (Keytruda)	• Pembrolizumab • Biomarker-targeted therapy: – Erdafitinib – Trastuzumab deruxtecan • Enfortumab vedotin • Avelumab (Bavencio) • Nivolumab (Opdivo)
Immunotherapy	• Biomarker-targeted therapy: – Erdafitinib – Trastuzumab deruxtecan • Carboplatin and Gemcitabine • Cisplatin and Gemcitabine • ddMVAC • Enfortumab vedotin • Enfortumab vedotin and Pembrolizumab	• Gemcitabine • Paclitaxel or Docetaxel
Chemotherapy and immunotherapy	• Enfortumab vedotin • Biomarker-targeted therapy: – Erdafitinib – Trastuzumab deruxtecan	• Cisplatin and Gemcitabine • ddMVAC • Enfortumab vedotin and Pembrolizumab • Gemcitabine • Paclitaxel or Docetaxel • Doxorubicin, Gemcitabine, and Ifosfamide • Gemcitabine and Paclitaxel

If your previous treatment included both immunotherapy and enfortumab vedotin, then the preferred next treatment options include chemotherapy combinations of ddMVAC, gemcitabine and cisplatin, or gemcitabine and carboplatin.

If you've had treatment with both chemotherapy and immunotherapy, the next preferred treatment option is enfortumab vedotin.

If testing finds your cancer has a certain biomarker, then you might have erdafitinib (Balversa) if it's a change in the *FGFR3* gene or trastuzumab deruxtecan (Enhertu) if it makes too much HER2 protein.

Other recommended treatments listed in **Guide 15** may be useful in certain situations, depending on the treatment you've already received.

Surgery for metastases

After systemic therapy, a small number of people may benefit from surgery to remove cancer that has grown in areas of the body other than the bladder (metastases). Surgery is most likely to help you if:

- Cancer isn't advancing quickly
- Systemic therapy was effective
- Metastases are limited to the lungs or lymph nodes
- Metastases are in only one area (only in the lungs, for example)

What's next?

After you've been treated for metastatic bladder cancer, you'll continue to have tests and visits to watch for cancer to return or progress, or to treat your existing cancer.

Surveillance is a key part of your follow-up plan. So be sure to go to follow-up visits and stay in touch with your care team. As always, you can ask to join a clinical trial.

Know that you can have bladder cancer and still enjoy life after diagnosis and treatment. Try to enjoy life as much as possible. Join a support group if you need additional resources.

Some people may reach a point where treatment stops working and there are no other treatments available. Even people who are still receiving treatment may feel sometimes like there's little hope. It's common to feel frustration, anger, regret, despair, and uncertainty—even all at the same time.

Talk with family or friends. Or talk to your doctor or another member of your care team. They can point you to professionals who can help you deal with these feelings and guide you toward your next steps.

Supportive care

Supportive care aims to improve your quality of life. It includes care for cancer symptoms and the side effects of cancer treatment. It also helps with other issues related to cancer.

For more information about supportive care, turn to *Chapter 8: Supportive care and other assistance*.

Key points

- Treatment of metastatic bladder cancer is focused on helping you live as normally and as comfortably as possible, for as long as possible.
- Talking about your diagnosis with doctors, nurses, therapists, or counselors, as well as other people with bladder cancer, can be helpful.
- Expect further testing to find out how many metastases there are and where they are in the body.
- The main treatment for metastatic bladder cancer is systemic therapy. Systemic therapies include chemotherapy, immunotherapy, and targeted therapy.
- Joining a clinical trial is strongly recommended for people with metastatic bladder cancer.
- Radiation therapy can be used to reduce symptoms and to ease the pain and discomfort of bladder cancer.

Questions to ask

- How will you know if the treatment is working? What are my options if the treatment stops working?
- How long do I have to decide about treatment? Is there a social worker or someone who can help me decide?
- Are you suggesting treatment options from the NCCN Guidelines, or have you modified the standard treatment in my situation?
- Are there any clinical trial options for me?



Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.
NCCN.org/patients/response

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Supportive care and other assistance

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Supportive care addresses the symptoms and side effects of bladder cancer, as well as psychological, social, financial, and spiritual issues. Many resources are available to help you feel better and answer your questions.

Supportive care

Supportive care is an important part of cancer care. The goal is to improve your quality of life during and after cancer treatment. Supportive care is for everyone with cancer and their families, not just for those at the end of life.

Supportive care includes a wide range of services. Supportive care prevents or manages the symptoms of cancer and the side effects of cancer treatment, like pain and cancer-related fatigue. It also addresses the mental, social, emotional, and spiritual concerns faced by people with cancer.

Supportive care provides help with additional needs, such as:

- Making treatment decisions
- Coordinating your care
- Paying for care
- Planning for advance care and end of life

Some health care professionals refer to palliative care as supportive care. They think these types of care are alike or overlap. Others think there are important differences, but both help people with cancer to live as well as they can.

Your cancer center may have palliative care specialists who can give you additional support and help coordinate your supportive care needs.

Read more about the types of support you may receive in *NCCN Guidelines for Patients: Palliative Care*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Anxiety and depression

Many people with cancer have symptoms of distress, such as anxiety and depression. You may feel anxious during testing, or you may experience depression during a hard part of treatment. Tell your treatment team so you can get help.

Help can include support groups, talk therapy, or medication. Cancer navigators, social workers, and other experts at your cancer center can help. Some people also feel better by exercising, talking with friends or loved ones, or relaxing.

Support groups

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment.

If your hospital or community doesn't have support groups for people with cancer, have a look at the online resources listed on page 80.

Financial concerns

The financial cost of bladder cancer can be overwhelming. Bladder cancer has the highest cost over a patient's lifetime of any cancer. As a result, many people with bladder cancer and their loved ones struggle with the cost of treatment, as well as the stress of paying for it.

To make things worse, you may miss work during treatment or become unemployed. Or you may have trouble paying for or getting medicines. Or you may have too little or no health insurance.

If you struggle to pay for food, housing, treatment, follow-up care, and other expenses, or you have difficulty getting to appointments, talk with your care team's social worker, patient navigators, and hospital financial services. They may be able to help you find financial support and transportation options.

You can also ask them about work, insurance, and managing medical costs.

If your doctor or other members of your care team don't talk about how to pay for treatment, it's okay for you to ask them about it first.

Advance care planning

When cancer is diagnosed very late or progresses despite all treatment efforts, it may be time to consider what lies ahead. This exploration of what's important to you is called advance care planning.

Advance care planning is for everyone, not just for those who are very sick. Even when cancer is curable, talking about future scenarios should begin when treatment is started.

Advance care planning means deciding what care you would want if you become unable to make medical decisions for yourself. It helps ensure that your wishes are understood and respected.

"Find a support network that understands your cancer type and the journey you are taking. Learning from others and having a safe place to ask questions is a huge benefit."



The advance care planning process starts with an open and honest discussion with your care team about your prognosis—what you may experience in the coming months—and the medications or therapies that may give you the best quality of life.

Quality of life refers to a person's overall enjoyment of life, including their sense of well-being and ability to participate in their usual activities.

This discussion should include your spouse or partner and other loved ones who are likely to be with you at the end.

Make your wishes clear. It's important that everyone clearly understands the goals of your care and your personal wishes about what should—and should not—be done.

You can decide if there's a point where you might want to stop cancer treatment. You can also decide what treatments you would want for symptom relief.

Once you've made these decisions, you'll fill out a legal document that explains what you want to be done if you aren't able to tell your care team yourself. This document is called an advance directive. Doctors are required to follow the instructions in an advance directive when you're too ill to make decisions about your care.

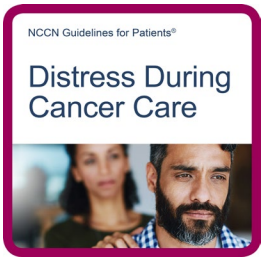
Tell your care team and family about your advance directive and its contents. Give a copy to all your doctors. Make sure you give a copy to anyone you've authorized to make decisions on your behalf (health care proxy).

It's okay to ask for help

Depression, anxiety, fear, and distress are very common feelings for people with cancer. These feelings can make it harder to deal with cancer and cancer treatment. They can hold you back even when you want to move forward.

Getting help when you're feeling worried or hopeless is an important part of cancer care. If you're feeling anxious or overwhelmed, ask your treatment team for help.

More information about cancer and distress is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



If your family or loved ones disagree with your plan, speak to your care team. Sometimes they or other specialists can help you and your family navigate these difficult conversations.

You can change your advance care plan at any time. Frequent conversations with your care team can help.

End-of-life considerations

End-of-life care provides medical, psychological, and spiritual support for people who are close to the end of life as well as those who love them. The goal is comfort, not cure. It may also be called comfort care or hospice.

Note that hospice is a special kind of end-of-life care. Hospice refers specifically to an insurance benefit for people whose life expectancy is 6 months or less. Hospice supports those at the end of life by bringing in additional care providers and resources such as home care.

The goal of end-of-life care is to give people the best life possible with the time they have left. Care can be provided in your home, a hospice facility, or even in the hospital.

A major goal is to keep you pain free and make sure that you can leave this world comfortably and with dignity. Hospice doctors, nurses, social workers, and chaplains are experts in helping patients work through the spiritual and emotional challenges of coping with the end of life.

Providing support for family members is a key part of hospice care. Most programs offer counseling and support groups for family members, including support after the patient has died. This is referred to as bereavement. It can be very comforting to know that your loved ones will have that kind of support after you're gone.



Tell your doctor if you're having any unusual feelings of sadness, loss of interest in activities, anxiety, or sleep problems. Many people experience these feelings, and they should not go untreated."

Key points

- Supportive care is for relieving symptoms, side effects, and other health issues related to cancer.
- Supportive care is treatment that involves the whole person, not just their cancer.
- Supportive care is given at any stage of disease, not just the end of life.
- If you're feeling distressed, ask about ways to reduce anxiety or depression.
- If you need financial support or transportation, talk with your care team's social worker, patient navigators, and hospital financial services.
- Advance care planning is done to ensure that your end-of-life wishes are understood and respected.
- Hospice care is for people who are close to the end of life. It's focused on comfort and quality of life.

Questions to ask

- Who can I talk to about feelings of sadness or anxiety?
- Can someone help me find a local or regional support group?
- Will my insurance cover the treatments you're recommending? How much will I have to pay myself?
- Does my insurance plan require preapproval before I start treatment?
- Who can I talk to about making an advance care plan?

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Other resources

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Want to learn more? Here's how you can get additional help.

What else to know

This guide helps you know your options so you can make informed decisions and improve your cancer care. But it's not the only resource that you have.

Ask for as much information and help as you need. Many people with bladder cancer are interested in learning more about:

- Finding a cancer specialist who's an expert in bladder cancer
- Shared decision-making and being a part of the cancer care team
- Living comfortably with a urinary diversion
- Chances for cancer recurrence
- Getting financial help
- Coping with other health problems

What else to do

Your health care center can help you with next steps. It often has on-site resources to help meet your needs and find answers to your questions. Health care centers can also inform you of resources in your community.

In addition to help from your providers, the resources listed in the next section provide support for many people like yourself.

Where to get help

Look through the list below and visit the provided websites to learn more about these organizations.

Bladder Cancer Advocacy Network
bcan.org

Cancer*Care*
cancercare.org

Cancer Hope Network
cancerhopenetwork.org

GRACE
cancergrace.org

Imerman Angels
imermanangels.org

PAN Foundation
panfoundation.org

Triage Cancer
triagecancer.org

United Ostomy Associations of America (UOAA)
ostomy.org

Urology Care Foundation
urologyhealth.org

Questions to ask

- Who can I talk to about help with housing, food, and other basic needs?
- What help is available for transportation, childcare, and home care?
- What other services are available to me and my caregivers?
- How can I connect with others and build a support system?
- Who can I talk to if I don't feel safe at home, at work, or in my neighborhood?



We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer. Take our survey to let us know what we got right and what we could do better.
NCCN.org/patients/feedback

Words to know

bacillus Calmette-Guérin (BCG)
An immunotherapy medicine put directly into the bladder to treat bladder cancer.

biopsy
A procedure that removes fluid or tissue samples to be tested for disease.

cancer grade
A rating of the difference between cancer cells and normal cells under the microscope. It's used to predict how fast the cancer is likely to grow or spread.

carcinoma in situ (CIS)
A flat area of cancer cells that hasn't grown any farther than where it started.

chemoradiation
Cancer treatment with both chemotherapy and radiation therapy.

chemotherapy
Cancer drugs that stop the cell life cycle to kill the cancer cells.

computed tomography (CT)
An imaging test that uses x-rays from many angles to make a series of pictures of the inside of the body.

continent urinary reservoir
Urinary diversion in which a portion of the large intestine is used as a pouch to hold urine. Also called an Indiana pouch.

cystectomy
Surgery that removes all or part of the bladder.

cystoscopy
A procedure to see inside the bladder using a special tool inserted through the urethra. Usually occurs in a procedure room in the doctor's office.

dose-dense chemotherapy
A method of speeding up chemotherapy by reducing the amount of time between treatments.

first-line therapy
The first type of treatment given for a condition or disease. First-line therapy is the one considered to be the best treatment.

hematuria
The presence of blood in urine.

ileal conduit
Urinary diversion in which a piece of small intestine (ileum) is used as a pipeline (conduit) for urine to leave the body through a hole (stoma) in the abdomen.

immunotherapy
Drug treatment that helps the body's immune system find and destroy cancer cells.

intravesical therapy
Treatment that uses a catheter to put medicine directly into the bladder.

magnetic resonance imaging (MRI)
An imaging method that uses radio waves and powerful magnets to make pictures of the inside of the body.

maintenance therapy
Therapy meant to prolong positive results after a good response to treatment, usually given before progression may occur.

metastasis
The spread of cancer from the place where it started to another part of the body.

muscle-invasive
Bladder cancer that has invaded the muscle layer of the bladder wall.

neobladder
Urinary diversion in which a piece of small intestine is made into a new urinary reservoir, which is connected directly to the urethra.

non–muscle-invasive
Bladder cancer that hasn't grown into the muscle layer of the bladder wall.

radiation therapy
Treatment that uses high-energy rays (radiation) to destroy cancer cells.

radical cystectomy
Surgery that removes the bladder, nearby lymph nodes, and other organs in the pelvis.

recurrence
The return of cancer after a cancer-free period.

resection
Surgery that removes as much cancer as possible while leaving the rest of the tissue or organ in place.

stage
A rating of the extent of cancer in the body.

surveillance
Ongoing testing after treatment to watch for the return of cancer.

systemic therapy
Treatment that works throughout the body.

targeted therapy
Treatment that can target and attack specific types of cancer cells.

transurethral resection of bladder tumor (TURBT)
Surgery to remove bladder tumors through the urethra without having to cut into the abdomen.

ureters
A pair of tubes that carry urine from the kidneys to the bladder.

ureteroscopy
A procedure that allows a doctor to see inside the kidneys and ureters using a special tool called a ureteroscope.

urinary diversion
Surgery that creates a new way for urine to leave the body after radical cystectomy.

urine cytology
A lab test performed on urine to detect cancer or precancerous cells.

urogram
An imaging method that creates detailed pictures of the kidneys, ureters, and bladder.

urothelial carcinoma
Cancer that begins in the urothelial cells that line the inside of the urinary tract.

urothelium
The stretchy inner lining of the bladder and other organs of the urinary tract.

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This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer, Version 2.2026. It was adapted, reviewed, and published with help from the following people:

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