NCCN GUIDELINES FOR PATIENTS®

2023

Bladder Cancer

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NATIONAL COMPREHENSIVE CANCER NETWORK®
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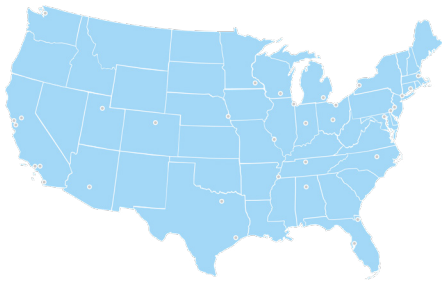
National Comprehensive Cancer Network®



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®).

Cancer care is always changing. NCCN develops evidence-based cancer care recommendations used by health care providers worldwide. These frequently updated recommendations are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). The NCCN Guidelines for Patients plainly explain these expert recommendations for people with cancer and caregivers.

These NCCN Guidelines for Patients are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer, Version 2.2023 – April 25, 2023.

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NCCN Foundation seeks to support the millions of patients and their families affected by a cancer diagnosis by funding and distributing NCCN Guidelines for Patients. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of innovation in cancer research. For more details and the full library of patient and caregiver resources, visit NCCN.org/patients.

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1
Bladder cancer basics

Having cancer can be worrisome and stressful. This book 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. This may reduce some of the fear and worry.

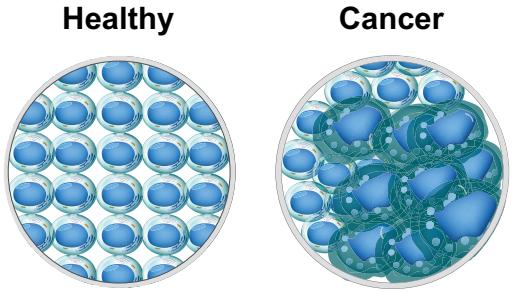
About bladder cancer

What is bladder cancer?

Bladder cancer is a disease that starts in the inner lining of the bladder. The bladder is a hollow, balloon-like organ that stores urine. It's located in your pelvis—the area between your hip bones in your lower abdomen. Bladder cancer happens when abnormal (cancer) cells in the bladder grow out of control. As cancer cells increase, they crowd out healthy cells.

Over time, the cancer cells may form a tumor in the bladder. Sometimes the cells grow deeper and invade the bladder's muscle wall. The cancer may even break through the bladder and spread to other parts of the body.

What is cancer?



Cancer is a disease where cells—the building blocks of the body—grow out of control. Cancer cells develop genetic errors (mutations) that cause them to make many more cancer cells. The cancer cells crowd out and overpower normal cells. This can end up harming the body.

Cancer cells also avoid normal cell death. They can spread to other areas of the body. They can replace many normal cells and cause organs to stop working.

Is bladder cancer common?

Bladder cancer is one of the most common cancers in adults. Most people who have bladder cancer are aged 55 years and over.

Bladder cancer is often found at an early stage when the cancer is highly treatable. However, bladder cancer commonly comes back again even after treatment. In many cases, bladder cancer comes back in a different place and sometimes worse than before. People with

bladder cancer need follow-up tests for many years to check if the cancer has returned.

The most common kind of bladder cancer starts in the urothelial cells, which are stretchy cells that line the inside of the bladder. Urothelial cells also form the inner layer in the rest of the urinary tract: the kidneys, the ureters, and the urethra. Urothelial cancer can start in these areas instead of the bladder, although it's rare.

Other types of bladder cancer—including squamous cell carcinoma, adenocarcinoma, and small cell carcinoma—are much less common.

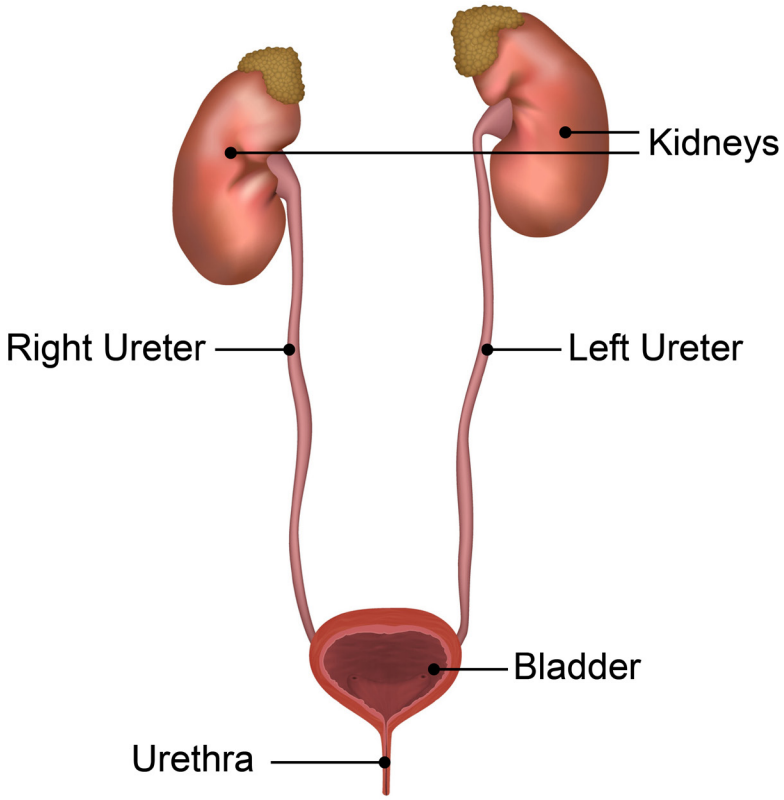
How is bladder cancer found?

Bladder cancer is usually found when a person has symptoms. A symptom is a problem or feeling that may signal a disease or condition. The most common symptom of bladder cancer, and the one that usually appears first, is having blood in your urine (hematuria).

How does blood get into urine? Bladder tumors are likely to leak blood, which mixes with the urine in your bladder. The blood may turn your urine pink or bright red. Or your urine may look normal if there isn't enough blood to be visible. The blood can still be found by looking at a urine sample under a microscope.

What does the bladder do?

- **The bladder is a hollow organ in the lower pelvis. Its main job is to store urine (pee). In adults, the bladder can hold up to 2 cups of urine.**
- **Urine is made by the kidneys and flows down to the bladder through two tubes called ureters.**
- **The bladder gets bigger as it fills with urine and gets smaller when you pee. It's about the size of an orange when empty and the size of a grapefruit when full.**
- **When you urinate, the muscles in the walls of the bladder contract. This forces the urine out of the bladder and through a tube called the urethra, which streams it out of the body.**
- **Together, these organs are called the urinary tract.**



Blood in the urine can be caused by many other things besides bladder cancer. The most common cause is an infection in the urinary tract. So anyone with blood in their urine should see a health care provider to get their urine tested.

Other symptoms of bladder cancer include:

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

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

A person with one or more of these symptoms should visit a doctor or other health care provider who can recommend different tests. These tests are used to make a diagnosis. (A diagnosis means identifying an illness by using tests.) Some people reading this book 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)
- Study your urine (urinalysis and cytology)
- Analyze a sample of surgically removed bladder tissue (resection and biopsy)

We'll talk about these and other tests in Chapter 2.

What causes bladder cancer?

Many people wonder why they got cancer. Scientists don't know exactly what causes bladder cells to grow out of control. What they do know is that bladder cancer and other cancers start with abnormal changes (mutations) in the genes of cells.

Genes are tiny parts of a cell that carry the instructions for how cells behave. These instructions also control how new cells are made. Sometimes, mutations can mix up these instructions. This can turn normal cells into cancer cells.

In most people with bladder cancer, these mutations aren't passed down in families (hereditary mutation). They happen on their own and only in cancer cells. Still, you may have a higher risk for bladder cancer if another family member also had bladder cancer.

In rare cases, mutations in these genes are passed down in families. This results in an increased risk of getting bladder cancer. However, only some individuals with these genetic mutations go on to develop bladder cancer.

What are the risk factors for bladder cancer?

A risk factor is something that increases your chance of developing a disease. Risk factors don't necessarily cause bladder cancer. But people with bladder cancer often have one or more of these risk factors:

- **Smoking** – Smoking is the greatest risk factor for bladder cancer. It accounts for about half of all cases. Quitting smoking after diagnosis can still be helpful.
- **Chemical exposure** – Some chemicals used in dyes, rubber, leather, printing

materials, textiles, and paint products have been linked to an increased risk for bladder cancer.

- **Age** – The risk of bladder cancer increases as you age.
- **Family history** – Your risk increases if you or anyone in your family has had bladder cancer. Also, people with an inherited condition called Lynch syndrome have a greater risk of cancer in the urinary tract, including bladder cancer.

How advanced is my bladder cancer?

Once bladder cancer is found, it's important to know how advanced it is. This means how far it has grown or spread. Bladder cancer advances in three phases:

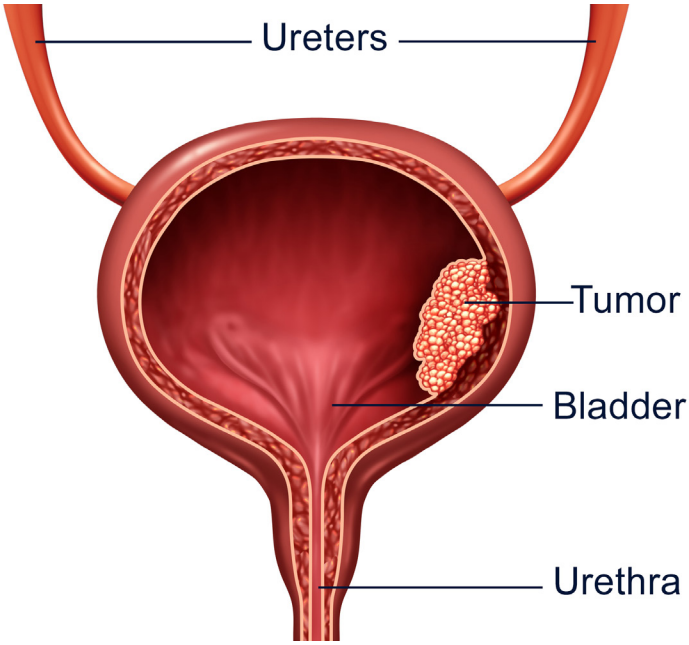
- **Non–muscle-invasive bladder cancer** has grown on or in the bladder's inner layer of urothelial cells, but not into the bladder's muscle wall.
- **Muscle-invasive bladder cancer** has grown through the bladder's inner urothelial layer and into its muscle wall.
- **Metastatic bladder cancer** has spread outside the bladder to other areas of the body. Common areas of metastatic bladder cancer include the lymph nodes, bones, lungs, liver, and the inner wall of the abdomen. (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.)

Treatment is different for each of these three phases of bladder cancer. These phases are further divided into stages, which are explained in Chapter 3.

Bladder cancer

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

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



Bladder cancer treatment

What's the best treatment for bladder cancer?

There's no single treatment that's best for everyone. The best treatment for bladder cancer is the treatment that's best for you. You'll work with your doctors and care team to choose which option makes the most sense for you. This choice 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, can be used for many types of bladder cancer. For less advanced cancer, a minor surgical procedure can be used to remove just the tumor. For more advanced cancer, the entire bladder can be surgically removed.

In addition, you may receive chemotherapy or immunotherapy directly into the bladder. For people with metastatic bladder cancer, chemotherapy or immunotherapy may be given as a whole-body treatment. Another treatment option is to join a clinical trial.

You'll also receive treatment for any side effects caused by cancer therapy.

What does aggressive mean?

When medical professionals describe cancer as aggressive, they mean the cancer is growing or spreading more quickly than average.

Aggressive is also used to describe a treatment that's stronger or more intense than usual.

Can bladder cancer be cured?

Bladder cancer in an early (non-invasive) stage can usually be cured. Treatment for more advanced stage (muscle-invasive) bladder cancer can be complicated but it may still get rid of the cancer. Metastatic cancer is not curable, but it can still be treated. For most people with bladder cancer, treatment provides a longer and more comfortable life with fewer symptoms.

It's important to know that bladder cancer commonly comes back even after treatment. In fact, bladder cancer is more likely to come back than almost any other kind of cancer. From now on, you and your health care providers will have to keep watching for any sign that the cancer returns.

Even so, there's hope. If the cancer does come back, it can be treated. Many people live with bladder cancer and still have a good quality of life.

Plus, new and improved ways to detect and treat bladder cancer are helping people live longer and with fewer side effects than ever before. Experts predict that treatment will improve rapidly over the next few years, with better results for all stages of bladder cancer.

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NCCN.org/patients/comments

Key points

- Bladder cancer happens when abnormal cells in the inner layer of the bladder grow out of control.
- Urothelial cell cancer is the most common kind of bladder cancer.
- The most common symptom of bladder cancer is blood in the urine.
- Bladder cancer comes from abnormal changes (mutations) in the genes of cells.
- Smoking is the greatest risk factor for bladder cancer.
- Many bladder cancers can be cured. All bladder cancers can be treated.
- For most people with bladder cancer, treatment requires more than one type of therapy.
- Bladder cancer very often comes back even after treatment. You and your care team will need to watch for its return for the rest of your life.

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.

2
Tests for bladder cancer

Several tests are needed to diagnose and treat bladder cancer. This chapter explains these tests and what to expect when being tested.

Before you can be treated, you'll need several tests to confirm your diagnosis. 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 comes back after treatment.

This chapter describes what tests you may have and what to expect during testing. Bring someone with you to listen, ask questions, and write down the answers.

Guide 1
Common tests and procedures for bladder cancer

Medical history and physical exam
Blood and urine tests
Cystoscopy and biopsy
Imaging of the pelvis or abdomen
Genetic testing
Questions about smoking

Tests and procedures that you may receive are listed in **Guide 1**. Not everyone will need all these tests.

General health tests

Medical and family history

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. Tell your doctor about any symptoms you have.

Some cancers and other diseases run in families. Your doctor will ask about the health history of family members who are blood relatives. This information is called a family history. Ask 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 enlarged glands (lymph nodes) in your neck, underarm, and groin.

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, which is removed through a needle placed into your vein. One sample may be used for several different blood tests:

Who's on your care team?

Treating bladder cancer takes a team approach. Some members of your care team will be with you throughout your cancer treatment, while others will be there for parts of it. Your team should communicate and work together to bring the best knowledge from each specialty. Get to know your care team and help them get to know you.

Depending on your diagnosis, your team may include a dozen or more health care providers:

Your primary care doctor handles medical care not related to your cancer. Your primary doctor can help you express your thoughts about treatments to your cancer care team.

A urologist is an expert in the urinary system and the male reproductive organs.

A urologic oncologist is a surgeon who diagnoses cancers of the urinary tract and the male reproductive organs, and treats the cancer using surgery and intravesical therapy.

A medical oncologist treats cancer using systemic therapies such as chemotherapy and immunotherapy. A medical oncologist will often coordinate your care with other team members. If not, ask who will coordinate your care.

A radiation oncologist prescribes and plans radiation therapy to treat cancer.

Oncology nurses provide your hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects.

A diagnostic radiologist reads the results of x-rays and other imaging tests.

An anesthesiologist gives anesthesia, a medicine so you don't feel pain during surgery or procedures.

Advanced practice providers are an important part of any team. These are registered nurse practitioners and physician assistants who monitor your health and provide care.

Residents and fellows are doctors who are continuing their training, some to become specialists in a certain field of medicine.

Nutritionists offer guidance on what foods or diet are most suitable for your particular condition.

Psychologists and psychiatrists are mental health experts who help manage issues such as depression, anxiety, or other mental health conditions that affect how you feel.

Genetic counselors are experts who interpret how your family history may impact your treatment.

Complete blood count

A complete blood count (CBC) measures the levels of red blood cells, white blood cells, and platelets in your blood. Your doctor 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.

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 areas like the kidneys or liver. Some important tests in a CMP are:

- **Liver function test** looks at enzymes made by the liver, like alkaline phosphatase and bilirubin.
- **Renal function test** measures waste products like creatinine and blood urea nitrogen (BUN) to check if your kidneys are working normally. This test can be very helpful for deciding your treatment.

Urine cytology

Urine cytology is a lab test that analyzes your urine for any 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 cystoscopy. 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) uses a microscope to look for any abnormal cells in your urine sample.

Tips for testing

Results from blood tests, imaging studies, and biopsies will be used to determine your treatment plan. It's important you understand what these tests mean. Ask questions and keep copies of your test results. Online patient portals are a handy way to access your test results.

Follow these tips for testing:

- ✓ Bring someone with you to doctor visits, if possible.
- ✓ Write down questions and take notes during appointments. Don't be afraid to ask your care team questions. Get to know your care team and help them get to know you.
- ✓ Get copies of blood tests, imaging results, and reports about the specific type of cancer you have.
- ✓ Organize your papers. Create files for insurance forms, medical records, and test results. You can do the same on your computer.
- ✓ Keep a list of contact information for everyone on your care team. Add it to your phone. Hang the list on your refrigerator or keep it in a place where someone can access it in an emergency. Keep your primary care physician informed of any changes.

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, or other areas.

Urine tests for tumor markers

Tumors shed cancer cells somewhat like a dog sheds hair. These cells can end up in urine. Urine tests are now available to identify some of these specific tumor cells. Scientists call these biomarkers.

At this time, biomarker tests may provide some helpful clues about bladder cancer, but aren't quite reliable enough to diagnose it. 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.

Cystoscopy and biopsy

Cystoscopy is a procedure to look inside your urethra and bladder for any sign of cancer. This procedure uses a cystoscope, a tube 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 the hospital, clinic, or doctor's office. The procedure takes only a few minutes, doesn't require anesthesia, and you can go home afterward.

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

The urologist will view a monitor that shows real-time images of the inside of the bladder.

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 tumors a little more distinctly than white light. A similar technology called narrow-band imaging also helps detect tumors more clearly during cystoscopy but doesn't require a dye.

While both blue light cystoscopy and narrow-band imaging have been shown to detect tumors better than standard white light, they're still relatively new and still in the "testing phase." More research will show whether they can replace white light as the standard detection method.

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.

If a tumor is visible, you'll need to have it removed in an operating room at a clinic or hospital. However, the urologist can completely remove very small cancer growths during the cystoscopy. This treatment is further explained in Chapter 4.

In a very similar exam, called a ureteroscopy, the cystoscope goes a little farther to examine parts of the upper urinary tract—the ureters and inner kidneys.

After a cystoscopy

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

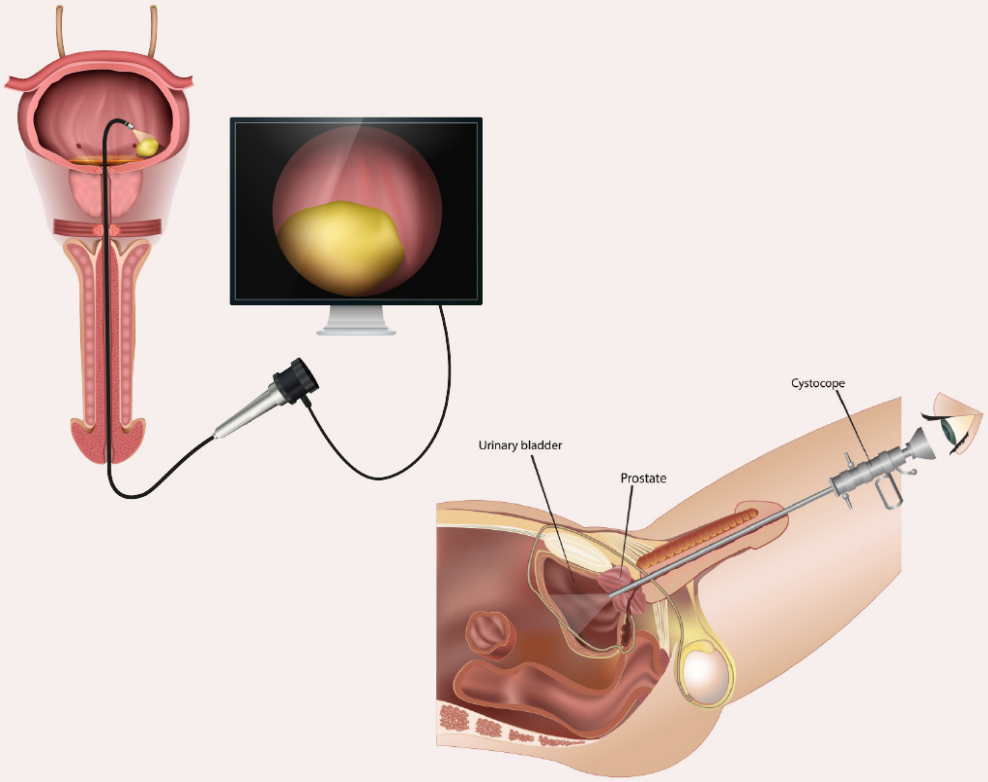
- Bleeding from your urethra, which can appear bright pink in your urine or on toilet paper
- A burning sensation during urination
- Urinating more often for the next day or two

If a tissue sample was taken for a biopsy, it will be sent to a lab and tested for cancer.

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).

A flexible cystoscope (upper left) is used for viewing and biopsy. A rigid cystoscope (bottom right) is more invasive, but it can also remove small tumors.



Imaging

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

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.

Types of imaging include x-rays, computed tomography (CT) scans, 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-ray pictures to make a single detailed image.

To look for cancer that has spread beyond the bladder, you may have a CT scan of your abdomen or 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.

A CT scanner is a large machine that has a 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.

Imaging

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

PET/CT scan

When a positron emission tomography (PET) scan is combined with CT, it's called a PET/CT scan. PET 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. A PET/CT scan can be done with one or two machines, depending on the cancer center.

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 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.

Because an MRI uses magnets, don't bring any metal objects (jewelry, cell phone, wristwatch, belts with metal buckles) 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 other parts of the urinary tract or other parts of the body:

- **Urogram** uses a contrast solution and either CT or MRI to see how well your entire urinary tract is working. The 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-ray to see if the cancer has reached the lungs.
- **Bone scan** is done when symptoms suggest that the cancer may have spread to any bones.

Inherited cancer risk

Sometimes, mutations in genes inherited from your parents can increase the risk for 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 or other features, your doctor might suggest genetic testing to find out if you have an inherited cancer risk.

The goal of this type of genetic testing is to look for germline (inherited) mutations that occur in every cell in your body. Germline testing may be more appropriate for people with bladder cancer 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

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 germline testing. 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. (See findageneticcounselor.com)

For bladder cancer, the most common germline mutations are found in these genes: *CDKN2A, FGFR3, PIK3CA, ERBB2.* If you have an inherited risk, your cancer might require additional testing or specialized treatment.

Quitting smoking is hard. Getting help can improve your chances of quitting for good.

Quitting smoking

Smoking increases the risk for bladder cancer. People who smoke are 3 times more likely to die from bladder cancer than people who don't smoke.

The more you smoke, the greater your risk. Quitting smoking may reduce your risk of getting cancer and other serious diseases.

It can also help the treatments for bladder cancer work better.

Key points

- Accurate testing is needed to diagnose and treat bladder cancer.
- 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.
- A urogram uses contrast and CT or MRI to see the lining of your urinary tract and to find out the extent of your bladder cancer.
- People who smoke are much more likely to die from bladder cancer than people who don't smoke.
- A urogram uses contrast and CT or MRI to see how well your urinary tract is working and to find out the extent of bladder cancer.
- People who smoke are much more likely to die from bladder cancer than people who don't smoke.

If you smoke or vape, seek help to quit

If you smoke tobacco or use e-cigarettes, it's very important to quit. Smoking can limit how well cancer treatment works. Smoking greatly increases your chances of having side effects during and after surgery. It also increases your chances of developing other cancers.

Nicotine is the chemical in tobacco that makes you want to keep smoking. Nicotine withdrawal is challenging for most people who smoke. The stress of having cancer may make it even harder to quit. If you smoke, ask your doctor about counseling and medicines to help you quit.

For online support, try these websites:

- SmokeFree.gov
- BeTobaccoFree.gov
- CDC.gov/tobacco

3
Staging and grading

The stage and grade of your cancer represent how far and how fast your cancer has grown. Your cancer stage describes how much cancer is in your body and where it's located. Your cancer grade conveys how aggressively your cancer is growing.

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 and 4 means it has grown through the bladder wall and out to 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).

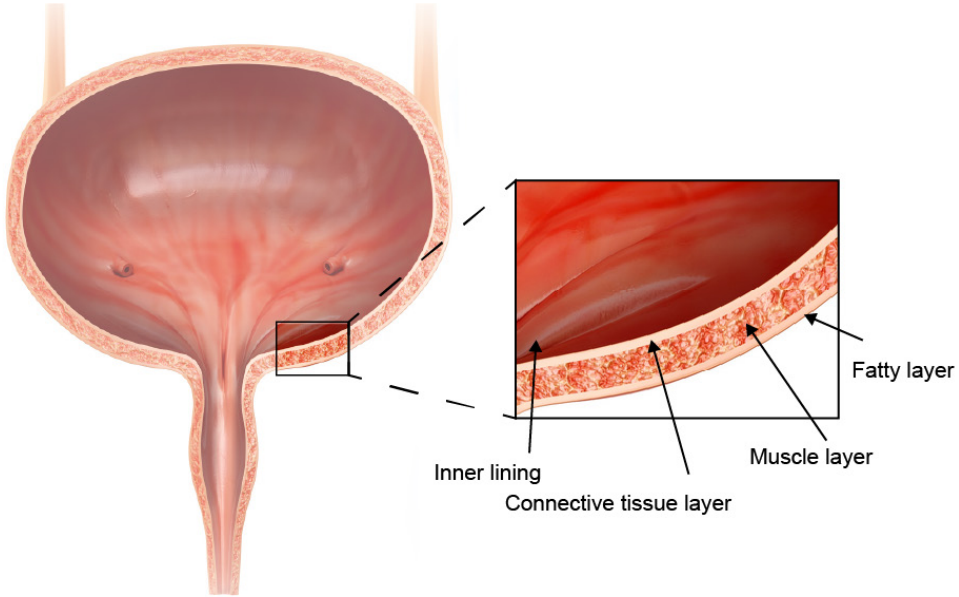
It's important for your care team to know the stage and the grade of your cancer to predict the course of your disease and to make a treatment plan.

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

Layers of the bladder

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

1. **Inner lining (or urothelium)**
2. **Connective tissue layer**
3. **Muscle layer**
4. **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.

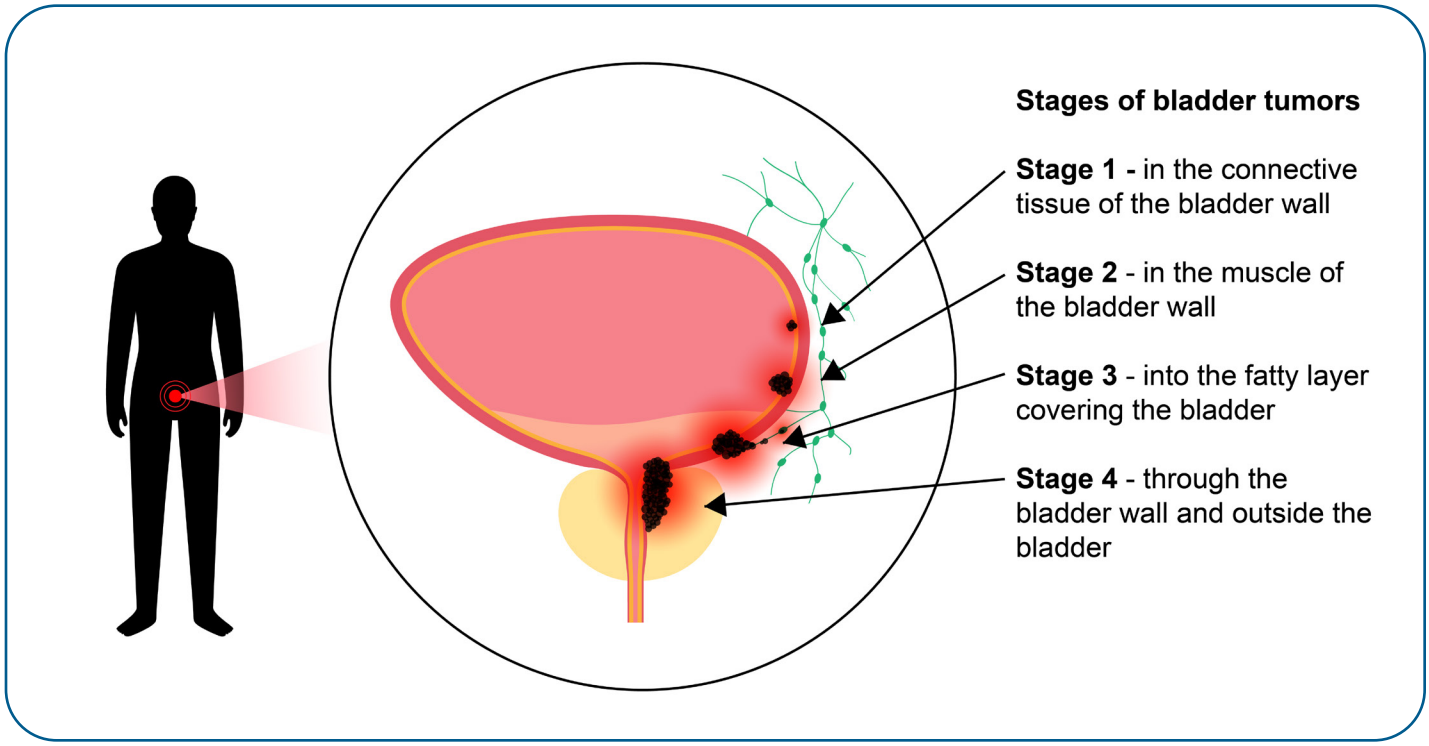
You may see the cancer stage written with a T, where the T stands for tumor: T0, T1, T2, T3, and T4.

An important thing about bladder cancer is whether the tumor has or hasn't grown into the bladder muscle. Cancer in stage 0 and stage 1 haven't grown into the muscle (non–muscle-invasive). Cancer in stages 2, 3, and 4 have grown into the muscle (muscle-invasive). Cancer that has invaded the muscle 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. 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, carcinoma in situ is fast-growing, aggressive, 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 tissue covering the bladder or 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 lymph nodes and organs nearby (in the pelvis). Stage 3 has two subgroups:

- **Stage 3A** bladder cancer may be only 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 that are far from the bladder.
- **Stage 3B** has the same traits as stage 3A but has spread to multiple lymph nodes in the pelvis. Stage 3B cancer has not spread to lymph nodes or organs far from the bladder.

Stage 4

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

- **Stage 4A** has invaded the wall of the pelvis or abdomen. Or, it has spread to lymph nodes far from the bladder.
- **Stage 4B** has spread to far away lymph nodes and organs like the bones, liver, or lungs. Stage 4B is metastatic bladder cancer.

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).

Variants

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 cell cancer has features that look like other types of cells. These are referred to as variants. Some of them include:

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

It's important to investigate whether you have one of these variants. In general, treatment for these uncommon variants is similar in the early stages to treatment for typical urothelial cancer. However, some variant subtypes might grow or advance faster than urothelial cell cancer. And faster growth might mean it needs more aggressive treatment.

Key points

- The stage of cancer is a rating to describe how deep it has grown into the bladder wall and how far it has spread. Cancer stage is used to determine which tests and treatments will help you receive the best outcome.
- An important thing about bladder cancer is whether it has or it hasn't grown into the muscle wall.
- There are five main stages of bladder cancer: 0, 1, 2, 3, and 4.
- Bladder cancer at stage 0 and stage 1 are non–muscle-invasive. Stage 0 means that abnormal cells have grown on the inside lining of the bladder. Stage 1 means that a tumor has formed and has invaded the layer of connective tissue in the bladder wall.
- Stages 2, 3, and 4 bladder cancers are muscle-invasive. The tumor has invaded the muscle layer of the bladder wall.
- 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 metastatic bladder cancer. This is cancer that has spread outside the bladder and to distant sites 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.
- Bladder cancer with variant features might need more aggressive treatment.

4

Treatment options for bladder cancer

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

Treatment for bladder cancer is based on many things. This includes 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. 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 treatment that affects the whole body, not just part of the body. Types of systemic therapy include chemotherapy, targeted therapy, and immunotherapy.
- **Radiation therapy** – Radiation therapy is a local therapy, which means it affects a specific area of the body. 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 resection and cystectomy.

Resection

For bladder cancer, a resection is a surgical procedure that removes the tumor but leaves the rest of the bladder in place. The full name of the procedure is called a transurethral resection of bladder tumor (TURBT, sometimes pronounced *turb-it*).

Even though it has a complicated name, the concept of TURBT is simple. It's a procedure that removes tumors through the urethra without having to cut into the abdomen. Tumor samples can also be tested to get a more detailed diagnosis.

TURBT is done in an operating room in a clinic or hospital. You'll be given anesthesia to put 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.

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

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

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. Or it may be done to get a deeper biopsy sample for the pathologist to examine.

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

Cystectomy

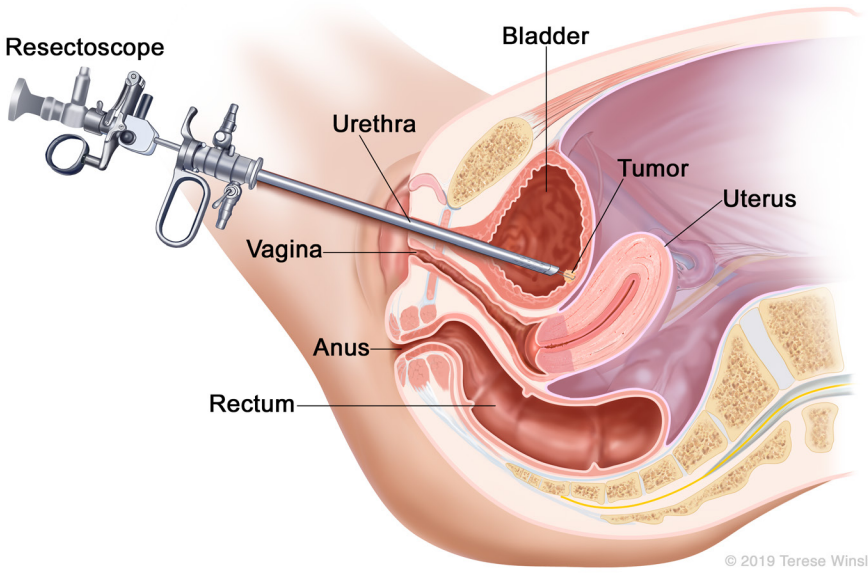
A cystectomy treats bladder cancer by removing the bladder. When the word radical is added, it means taking out the whole bladder as well as nearby lymph nodes and perhaps other nearby organs, including:

- Urethra
- Prostate
- Seminal vesicles (glands that help make semen)
- Part of the vas deferens (a tube that carries sperm away from the testicles)
- Proximal urethra (part of the urethra that goes through the prostate)
- Uterus

TURBT

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

Transurethral Resection of Bladder Tumor (TURBT)



- Ovaries
- Fallopian tubes
- Part of the vagina

Radical cystectomy is the most widely used surgery for muscle-invasive bladder cancer. It's a major operation that involves cutting into your abdomen. You'll need to stay in the hospital for at least several days. It may take 2 to 3 months or longer for you to recover. Talk to your urologist and treatment team about the risks, benefits, and side effects of a radical cystectomy.

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 also done at the same time.

To find out about the 3 types of urinary diversions, **see the next page.**

Partial cystectomy

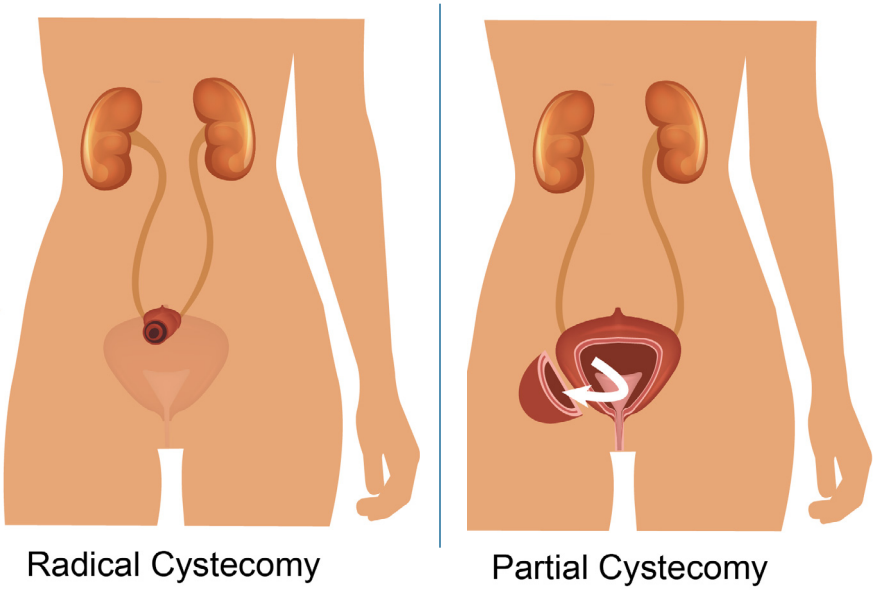
A partial cystectomy is a surgical procedure to remove part of the bladder. It's not widely used for the treatment of bladder cancer. Fewer than 5 out of 100 people with bladder cancer are eligible for a partial cystectomy. It can only be done if the cancer is in a spot that can be neatly removed without 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 diversion:

Ileal conduit

In this urinary diversion, the surgeon removes 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 attached to 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 called a wafer. The wafer 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.

Continent cutaneous 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. Sometimes the stoma can be made in the belly button, making it much less noticeable. A catheter must be inserted into the stoma, through the valve, and into the pouch several times a day to drain the urine.

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.

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.

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 using a process called instillation.

The two main intravesical therapies used to treat bladder cancer are intravesical bacillus Calmette-Guérin (BCG) and intravesical 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. Intravesical BCG can lower the chance of recurrence (cancer coming back) or getting worse (invading bladder muscle).

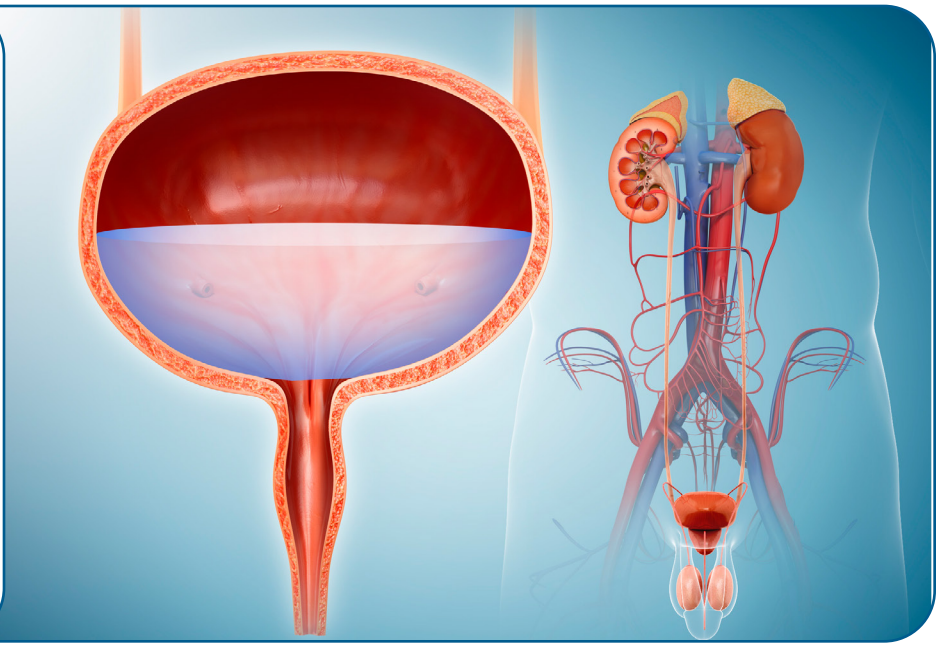
Intravesical BCG is commonly used for high-grade bladder cancer that hasn't invaded the muscle wall. It's usually started about 3 to 6 weeks after TURBT, to allow the bladder time to heal. It's given once a week for 6 weeks. You should have a full re-evaluation at 12 weeks after starting treatment.

To prevent recurrence, you might be asked to continue having intravesical BCG therapy. This is called maintenance therapy. Maintenance therapy involves three intravesical BCG treatments (given in one week) at 3 months and again at 6 months after TURBT. 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, and blood or particles (clots) in urine. Talk to your

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.



treatment team about the side effects. There may be ways to help lessen these effects.

Intravesical chemotherapy

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

Intravesical chemotherapy can be given right after a TURBT procedure. The treatment is a one-time dose instilled within 24 hours of TURBT surgery. It's meant to "clean up" 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 were given 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. Maintenance intravesical chemotherapy, if given, is usually on a monthly basis.

Chemotherapy drugs used for intravesical treatment include gemcitabine or mitomycin, among others. Gemcitabine is commonly chosen because it has fewer side effects and is less likely to be absorbed into the blood than mitomycin.

Because intravesical chemotherapy only goes into the bladder, 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.

BCG shortage

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 several years. As a result, many people with non–muscle-invasive bladder cancer haven't been able to receive this treatment or have received a reduced dose. 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 (such as gemcitabine or mitomycin). Other options include:

- ✓ Reduced doses or a shorter course of BCG treatment
- ✓ Intravesical treatment with a different chemotherapy medicine
- ✓ Bladder removal surgery (for those at high risk of the cancer returning after treatment)
- ✓ Joining a clinical trial

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 doctor 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.

Note that **systemic** chemotherapy is different than **intravesical** chemotherapy. Systemic chemotherapy is a whole-body therapy. Intravesical chemotherapy only affects the inside of the bladder.

Chemotherapy

Chemotherapy is treatment with drugs to kill cancer cells. Most 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 or sometimes after surgery depending on your type or stage of bladder cancer. Chemotherapy alone (without surgery) is sometimes the main treatment for people with metastatic bladder cancer.

The most used chemotherapy for bladder cancer combines four medicines. One of these is cisplatin, which contains the metal platinum.

What is dose-dense chemotherapy?

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

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 treatment called a cycle. A 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 treatment cycle is then repeated a few times. For example, you might have 3 to 6 cycles of chemotherapy over 2 to 3 months.

Immunotherapy

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

Checkpoint inhibitors are one type of immunotherapy used to treat bladder cancer and other cancers. Checkpoint inhibitors block cancer-boosting proteins called checkpoints.

The checkpoint inhibitors for bladder cancer include:

- Keytruda (pembrolizumab)
- Opdivo (nivolumab)
- Bavencio (avelumab)
- Tecentriq (atezolizumab)

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.

Targeted therapies for certain types of bladder cancer include:

- Balversa (erdafitinib) is a targeted therapy used for people whose bladder cancer is due to specific mutations in the *FGFR2* and *FGFR3* genes.
- Padcev (enfortumab vedotin-ejfv), which targets and attaches itself to a specific protein, Nectin-4, found on the surface of bladder cancer cells.
- Trodelvy (sacituzumab govitecan-hziy) also seeks and latches onto a protein, Trop-2, found in large numbers on cancer cells.
- Adstiladrin (nadofaragene firadenovec-vncg) delivers a gene, interferon alfa-2b, into bladder cells. The gene kickstarts the bladder cells to make an abundance of a natural protein that fights cancer. Adstiladrin is a gene therapy, but it's only used in certain cases of non–muscle-invasive bladder cancer that are difficult to treat.

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

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 at the tumor area.

Radiation therapy can be given alone but is more often given with other bladder cancer treatments:

Chemoradiation

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

Trimodal therapy

Trimodal therapy refers to a combination of three 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 bladder removal surgery (radical cystectomy). This is why trimodal therapy is referred to as a "bladder preserving" treatment.

Clinical trials

Therapy may also be given as part of a clinical trial. A clinical trial is a type of medical research study and a vital way to assess new treatment methods.

After being developed and tested in a laboratory, 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. Food and Drug Administration (FDA).

Everyone with cancer should carefully consider all 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. Treatment trials are done in phases.

- **Phase 1** trials study the dose, safety, and side effects of an investigational drug or treatment approach. They also look for early signs that the drug or approach is helpful.
- **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 long-term safety and benefit of an FDA-approved treatment.

Who can enroll?

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. These requirements ensure that participants are alike in certain ways in order to compare how they respond to a specific treatment.

Informed consent

Clinical trials are managed by a group of experts called a research team. The research team 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. This agreement confirms that you've been fully told about your part in the trial. Read the form carefully and ask questions before signing it. Take time to discuss it with family, friends, or others you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

Start the conversation

Don't wait for your doctor to bring up clinical trials. Start the conversation and learn about all your treatment options. Ask if a clinical trial is available for your situation. If you find a study that you may be eligible for, ask your treatment team if you meet the requirements. If you have already started standard treatment, you may not be eligible for certain clinical trials. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

Frequently asked questions

There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

Will I get a placebo?

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

Are clinical trials free?

There's no fee to enroll in a clinical trial. The study sponsor usually pays for research-related costs, including the study drug. Health insurance plans aren't required to cover the research costs of a clinical trial. You may, however, have costs indirectly related to the trial, such as the cost of transportation or childcare due to extra appointments.

Depending on the trial, you may continue to receive standard cancer care. The standard treatment is billed to—and often covered by—insurance. You're responsible for copays and any costs for this care that aren't covered by your insurance.

Supportive care

Supportive care is health care that relieves symptoms caused by cancer or by its treatment. The aim of supportive care is to improve your quality of life. Supportive care may include relieving symptoms, emotional or spiritual support, financial aid, or family counseling.

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

Supportive care is available at any cancer stage. Speak to your care team about how you're feeling and if you're having any side effects. You can read more about supportive care in Chapter 8.

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 while others can be 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 of treatment (radiation versus chemotherapy, for example) and the length or the dose of treatment. Here are some common side effects of different treatments:

Bladder removal surgery – bleeding, blood clots, kidney problems, infection, sexual dysfunction, incontinence, problems caused by the urinary diversion

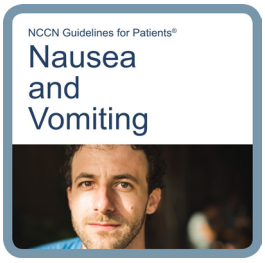
Intravesical therapy – swelling (inflammation) of the bladder lining, frequent urination, pain or burning feeling when urinating, blood in the urine, infection

Chemotherapy – nausea, vomiting, extreme tiredness (fatigue), fever, infection, tingling or numbness, rash, diarrhea

Immunotherapy – autoimmune reaction, 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** – Treatment or cancer itself 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.

Key points

- Treatment options for bladder cancer depend on the stage and grade of your cancer, your overall health, and your preferences.
- Transurethral resection of bladder tumor (TURBT) is a procedure that examines tumors on the bladder wall and removes them.
- Radical cystectomy is the most widely used surgery for muscle-invasive bladder cancer. It involves removing the bladder, nearby lymph nodes, and other organs in the pelvis.
- A partial cystectomy is a surgical procedure to remove part of the bladder. It's rarely used for the treatment of bladder cancer.
- A urinary diversion is a surgical procedure included 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 through a catheter. The medicine is slowly put into the bladder using a process called instillation.
- A cancer treatment that affects the whole body is called systemic therapy. The most common types of systemic therapy are chemotherapy and immunotherapy.
- Chemotherapy is treatment with drugs to kill cancer cells. Most chemotherapy drugs are liquids that are slowly injected into a vein (infusion). Chemotherapy affects cancer cells (and other cells) throughout the whole body.

Strength is needed to sustain you during treatment. Take care of yourself by eating well, drinking plenty of fluids, exercising, and doing things that make you feel energized.

- Targeted therapy drugs can pick out and attack specific types of cancer cells. But they're only useful in certain cases.
- Immunotherapy drugs called checkpoint inhibitors are used to treat bladder cancer.
- Chemotherapy and radiation therapy are often used at the same time to treat bladder cancer. They can work better together than they do separately.
- A clinical trial is a medical research study that investigates potential new ways of fighting cancer.
- All treatments for bladder cancer can cause side effects. Ask your care team about ways to deal with the side effects of treatment.

What's your cancer 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 you 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.

Your overall cancer stage	Chapter	Page
0	5. Non–muscle-invasive	40
0a	5. Non–muscle-invasive	40
0is	5. Non–muscle-invasive	40
1	5. Non–muscle-invasive	40
2	6. Muscle-invasive	47
3A	6. Muscle-invasive	47
3B	6. Muscle-invasive	47
4A	6. Locally advanced/metastatic	47
4B	7. Metastatic	62

5

Treatment for non–muscle-invasive bladder cancer

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 cancers are non–muscle-invasive. Often, non–muscle-invasive bladder cancer can be treated without removing the bladder.

Stage 0 and stage 1 bladder cancers

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

- **Stage 0a** (also called noninvasive papillary carcinoma) are 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.

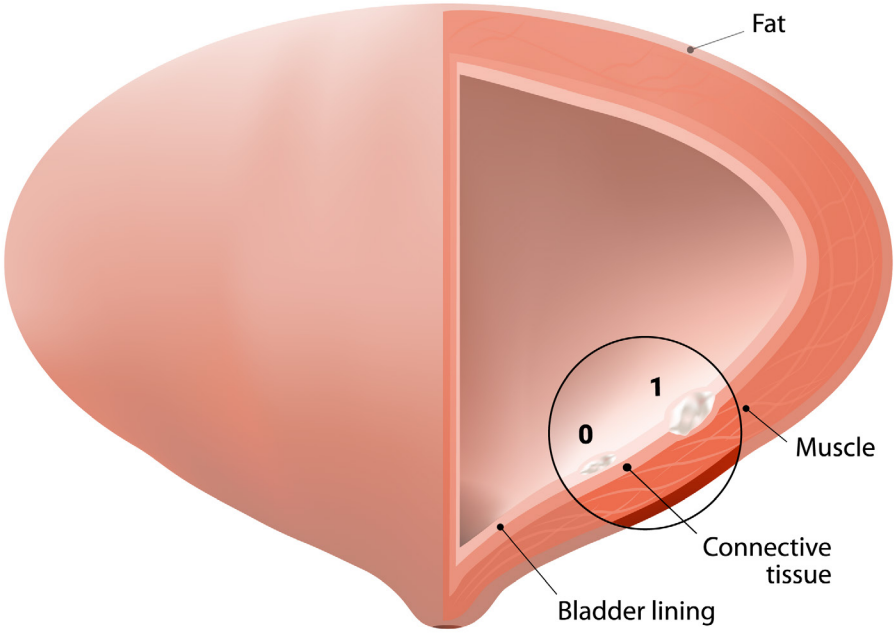
Stage 1 bladder cancer has grown into the layer of connective tissue of the bladder wall but hasn't reached the muscle layer.

Treatment for stage 0 and stage 1 bladder cancers depends on whether the cancer has low, medium, or high risk for coming

Stage 0 and stage 1 bladder cancers

Stage 0 bladder cancer is only on the inner lining of the bladder wall.

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



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

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 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 include 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.**

Guide 2
Stage 0 and stage 1 treatment options

Low risk	• Small, single, slow-growing stage 0a lesion	→	• Surveillance
Medium risk	• Large or multiple slow-growing stage 0a tumor(s) • Slow-growing stage 0a tumor that comes back within 1 year • Small, single, fast-growing stage 0a tumor • Slow-growing stage 1 tumor	→	• Intravesical (BCG or chemo) therapy* • Surveillance
High risk	• Large or multiple fast-growing stage 0a tumor(s) • Fast-growing stage 0is tumor • Fast-growing stage 1 tumor	→	• Intravesical BCG therapy* • Radical cystectomy
	• Stage 0 or stage 1 tumor with very high risk features	→	• Radical cystectomy* • Intravesical BCG therapy

**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. **See Guide 2** again.

- **Low risk** bladder cancer care is surveillance. Surveillance means watching out for cancer to reappear after it's been treated. For stage 0 bladder cancer, surveillance usually involves follow-up cystoscopy and urine cytology tests every 3 to 6 months for 2 years or more.
- **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 (BCG or chemotherapy).
- **High risk** bladder cancer has a major risk of coming back or growing further. High risk cancer is typically treated with intravesical BCG therapy (if you haven't had BCG before), although radical cystectomy is also an option.
- **High risk bladder cancer with very high-risk features** has a greater chance of progressing to an advanced stage, so radical cystectomy is the preferred treatment. Additional treatment options in certain cases are intravesical chemotherapy, Keytruda (pembrolizumab), or Adstiladrin (nadofaragene firadenovec-vncg). Very high-risk features include:
  - Intravesical BCG therapy has no effect on it.
  - Tumor cells are found in the blood or in lymph vessels outside of the main tumor (lymphovascular invasion).
  - Cancer recurrence develops in the urethra.
  - The cancer is a rare subtype that usually leads to poor outcomes (variant features).

Supportive care should also be available during treatment. Supportive care is for relieving symptoms and for other concerns.

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 book, bladder cancer often comes back at some point. So, surveillance is always recommended after treatment ends. Make sure you go to all your follow-up appointments. (Of course, 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 for cancer recurrence. Each person's follow-up plan is different. Depending on your type of cancer and other health considerations, you may need to have these follow-up tests:

- Cystoscopy
- Imaging of upper urinary tract
- Imaging of abdomen and pelvis
- Urine cytology
- Urinary biomarkers

If you didn't have your bladder removed as part of your treatment, **see Guide 3** for follow-up testing based on your risk level.

If your bladder was removed, see which follow-up tests you'll need in **Guide 4.**

Recurrence or progression

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

If cancer returns during follow-up therapy, it's usually detected by a cystoscopy exam.

Guide 3
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	**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
Imaging of abdomen and pelvis	**Year 1:** Baseline imaging with CT or MRI **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.

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. (Like your first TURBT, you'll probably also have a single dose of intravesical chemotherapy with the repeat TURBT.) The level of risk indicates the appropriate treatment. **See Guide 2.**

For example, if the repeat TURBT shows that the cancer has come back as high risk non–muscle-invasive cancer, the preferred treatment is intravesical BCG therapy. Radical cystectomy is also an option, especially if you've had BCG therapy before and it didn't reduce the cancer. After this treatment, you'll resume follow-up.

Guide 4
Follow-up tests after bladder removal 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>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</td><td rowspan="4">As directed by your doctor:
• Urine cytology
• Urethral wash cytology (only if high risk of recurrence)</td></tr>
<tr><td>Year 3</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</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>

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, and/or prostate
- Urine cytology of the upper urinary tract
- Ureteroscopy, a test that examines the insides of the kidneys and ureters

If the biopsy of the bladder finds cancer, intravesical BCG therapy is recommended. If BCG therapy works and cancer is no longer found, you may continue with maintenance BCG therapy to prevent recurrence.

If BCG therapy doesn't clear away the cancer, then treatment options include:

- Radical cystectomy
- A different intravesical therapy
- Clinical trial
- Immunotherapy with Keytruda or Adstiladrin (only for certain patients with stage 0is cancer)

Treatment for other test results:

- If a biopsy of the prostate finds cancer, then testing and treatment of the prostate is needed.
- If a urine cytology of the upper tract indicates cancer, then you'll need testing and treatment of the upper urinary tract.
- If none of the tests detect cancer, you should have a follow-up visit in 3 months. Other visits will be spaced farther apart.

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

Key points

- Many non–muscle-invasive cancers can be treated without removing the bladder.
- Treatment for non–muscle-invasive bladder cancer is based on the risk that the cancer will come back or continue to grow.
- You'll need another TURBT if the first TURBT didn't remove enough of the tumor or didn't include any muscle tissue from the bladder wall.
- Surveillance is often the best care for low risk bladder cancer. Surveillance means occasional testing to find out if cancer has returned.
- The preferred treatment for medium risk bladder cancer is intravesical therapy with either BCG or chemotherapy.
- High risk cancer is typically treated with intravesical BCG therapy, although radical cystectomy is also an option.
- Radical cystectomy is the preferred treatment for high risk bladder cancer with very high risk features.
- Follow-up testing is based on the risk of the cancer returning. The higher the risk, the more tests are needed.

6

Treatment for muscle-invasive bladder cancer

If the tumor grows large enough to reach the thick layer of muscle in the bladder wall, it's called muscle-invasive bladder cancer. 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, you can turn to the page that describes the treatment for that stage.

Stage 2 and stage 3A bladder cancers

Stage 2 bladder cancer has grown into the muscle layer, but it hasn't reached the fatty tissue covering the bladder or spread anywhere else. Stage 2 bladder cancer has a better prognosis than cancer that has reached the fatty layer and beyond.

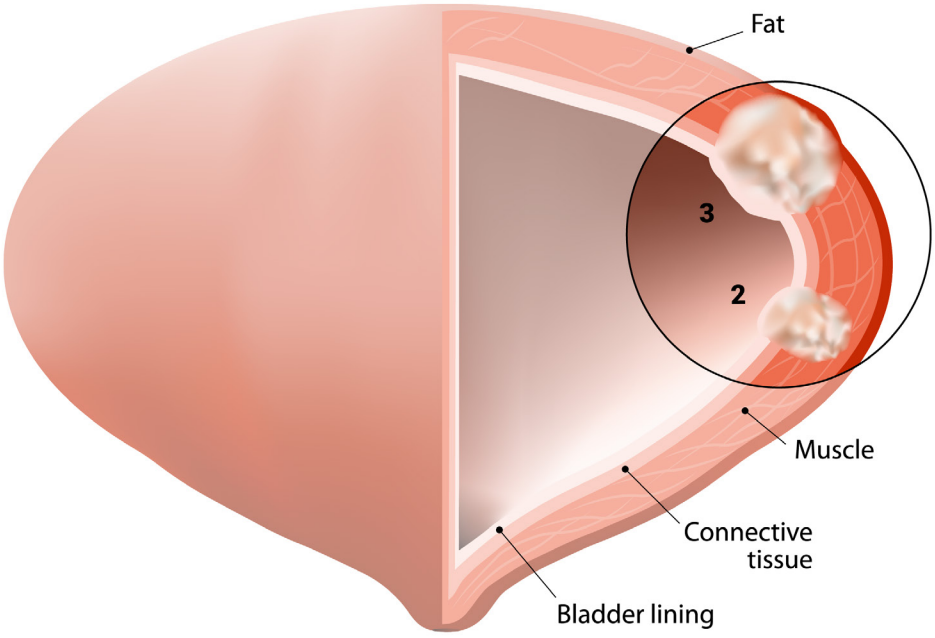
Stage 3A bladder cancer has grown through the bladder wall to the fatty layer surrounding the bladder. It may have spread to nearby reproductive organs such as the prostate gland, seminal vesicles, uterus, or vagina. Or, it may also have spread to a single nearby lymph node. Stage 3A cancer has not spread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

The main treatment for stage 2 and stage 3A bladder cancers is a radical cystectomy. This is a surgery that removes the cancer

Stage 2 and stage 3A bladder cancers

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.



by taking out the entire bladder and nearby lymph nodes, as well as the prostate or uterus. Combination chemotherapy with cisplatin is often given beforehand to shrink the tumor prior to the surgery and to kill any cancer cells that might be outside the bladder.

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 undergo a 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 process and get rid of any chemotherapy drugs.

Some people with stage 2 bladder cancer can't have surgery or don't want it. If this describes you, you can skip the next section and go directly to *Treatment without bladder removal* on page 50.

Bladder removal surgery

Radical cystectomy can be done with or without cisplatin-based chemotherapy. The choice depends on whether you're able to have the chemotherapy.

Chemotherapy and bladder removal surgery

This option starts with a combination of chemotherapy drugs, one of which is cisplatin. Cisplatin has been shown to be the most effective chemotherapy for treating bladder cancer. Typically, 3 to 6 cycles of chemotherapy are given before bladder removal surgery. For recommended chemotherapy options, **see Guide 5.**

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.

Bladder removal surgery alone

This is an 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 if you're

Guide 5
Stages 2 and 3A chemotherapy options before bladder removal surgery

dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin (ddMVAC)*	3–6 cycles
gemcitabine and cisplatin	4 cycles

** Preferred treatment.*

not able to do most daily activities, then you too may not be able to have cisplatin-based chemotherapy.

People who can't have cisplatin don't need to try different or less effective chemotherapy. Bladder removal surgery is the most appropriate option.

Treatment after surgery

Depending on what the surgeon sees and learns first-hand during radical cystectomy, you may have additional therapy to try to destroy any remaining cancer cells. Reasons why you may need additional therapy include:

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

The choice of additional treatment is based in part on whether you received therapy before surgery. **See Guide 6**. Treatment options include:

- Cisplatin-based chemotherapy (if you didn't have chemo before surgery)
- Immunotherapy with Opdivo (if you had chemo before surgery)
- Radiation therapy (in selected patients whose tumor was larger and/or reached the lymph nodes)

Follow-up

For recommendations on follow-up care and monitoring for the return of cancer, see page 58.

Treatment without bladder removal

There are several reasons why you may be unable 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, you may simply not want to have a cystectomy. Bladder cancer treatment that doesn't involve radical cystectomy is called "bladder preserving."

There are three treatment options that don't involve removing the bladder:

Trimodal therapy

Trimodal therapy is a bladder preserving treatment for certain people with muscle-invasive bladder cancer. In trimodal therapy, TURBT 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 7** 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 radical cystectomy, radiation therapy alone is a possible treatment option for stage 2 or stage 3A bladder cancer.

TURBT

Having only TURBT treatment may be an option for people who can't have, or don't want, radical cystectomy. This option may work better if the tumor is smaller than 2 centimeters (about the size of a penny or a grape). Within 4 weeks of the TURBT, you should have a repeat TURBT to make sure there's no cancer left behind.

What's next?

The tumor should be checked 2 to 3 months after you've finished treatment. Depending on

Guide 6
Stages 2 and 3A treatment options for bladder removal surgery

Treatment options

- **Chemotherapy and bladder removal surgery** with urinary diversion
- **Bladder removal surgery alone** with urinary diversion

Additional treatment options

- If tumor is stage 2 or smaller, and
- No cancer in lymph nodes

→ **No additional therapy needed**

- If the tumor is larger than stage 2, or
- If the tumor has invaded muscle layer, or
- If cancer is found in lymph nodes

→ **Additional therapy needed:**

- Cisplatin-based chemotherapy (if not given before)
- Immunotherapy (Opdivo)
- Radiation therapy (in selected cases)

For stage 2 cancer, partial bladder removal is possible but uncommon.

Guide 7
Can you have bladder preserving treatment?

Common characteristics

Chemoradiation without bladder removal surgery is an option only for some people with muscle-invasive bladder cancer.

Every person is different, but here are some common characteristics of those who can have bladder-preserving treatment:

→

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

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 for the return of cancer.

If cancer is still there and you can have radical cystectomy, treatment options are based on the type and of size the remaining tumor. Options include TURBT with or without intravesical therapy if the tumor is now stage 1, radical cystectomy 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 radical cystectomy, treatment options include cisplatin-based chemotherapy, TURBT with or without intravesical therapy, and supportive care. For stage 2 bladder cancer, radiation therapy alone is also an option if you didn't have it before.

Follow-up

For recommendations about follow-up care and monitoring for the return of cancer, see page 58.

Stage 3B bladder cancer

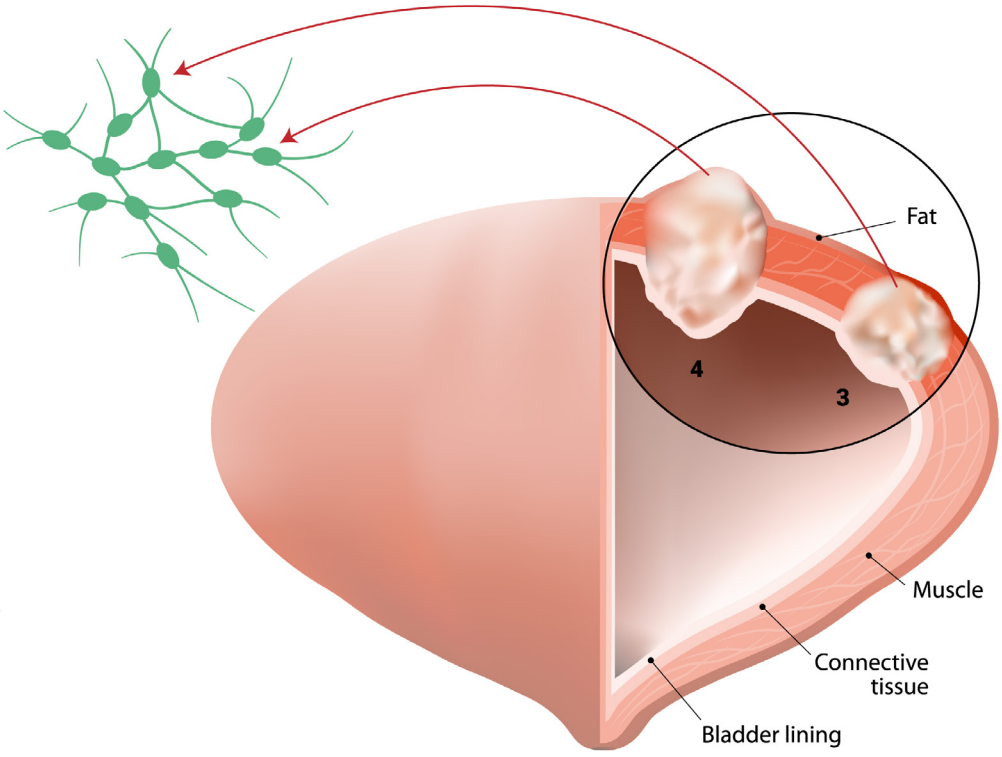
Stage 3B bladder cancer is considered locally advanced. This means the cancer has grown outside the bladder and spread to multiple lymph nodes in the pelvis or to at least one lymph node in the upper pelvic region. But the cancer has not spread to organs or lymph nodes far from the bladder.

The main treatment options for stage 3B bladder cancer are chemotherapy or chemoradiation. Additional treatment may be needed depending on how well the main therapy works.

Stage 3B and stage 4A bladder cancers

Stage 3B bladder cancer has grown outside the bladder and spread to nearby lymph nodes or those in the upper pelvis.

Stage 4A has grown through the bladder wall. It may have spread to the wall of the pelvis or the abdomen. It may also have spread to nearby and even to distant lymph nodes.



Chemotherapy

Chemotherapy is used to shrink the tumor as much as possible and kill any cancer cells outside of the bladder. Treatment depends on whether you can tolerate chemotherapy with the drug cisplatin. Cisplatin has been shown to be the most effective chemotherapy for treating bladder cancer. Typically, 3 to 6 cycles of combination chemotherapy are given.

Guide 8
Systemic therapy options for stage 3B and stage 4A bladder cancers

Can you have cisplatin?	Systemic treatment options	Drug type	Maintenance therapy afterward
Yes, I can have cisplatin	gemcitabine and cisplatin*	Chemotherapy	Bavencio (avelumab) immunotherapy
	dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin (ddMVAC)*	Chemotherapy	Bavencio (avelumab) immunotherapy
No, I can't have cisplatin	gemcitabine and carboplatin*	Chemotherapy	Bavencio (avelumab) immunotherapy
	Keytruda (pembrolizumab)*	Immunotherapy	none
	Padcev (enfortumab vedotin-ejfv) and Keytruda (pembrolizumab)*	Targeted therapy and immunotherapy	none
	gemcitabine	Chemotherapy	none
	gemcitabine and Taxol (paclitaxel)	Chemotherapy	none
	Tecentriq (atezolizumab) - *only if your cancer has PD-L1 biomarker*	Immunotherapy	none
	ifosfamide, doxorubicin, and gemcitabine – *only if you have good kidney function and good activity level*	Chemotherapy	none

** Preferred options.*

If you can't have cisplatin, other chemotherapy, immunotherapy, and targeted therapy medicines are available for stage 3B cancer. For recommended systemic therapy options, **see Guide 8.**

About 2 to 3 months after you've finished therapy, you'll have imaging tests to see if the treatment worked. If the tests show that the cancer didn't grow or spread after either platinum-based chemotherapy or chemoradiation, you can have maintenance treatment to retain the benefits of therapy and to slow the cancer from growing. Bavencio (avelumab), a checkpoint inhibitor, is the preferred maintenance option.

If no cancer is found after initial treatment, your next step depends on your specific circumstances:

- Monitoring without additional treatment. This doesn't mean the cancer has been cured. You would begin follow-up and monitoring for the return of cancer.
- Additional therapy to wipe out any undetectable cancer cells that may be left behind. This is called consolidation therapy. Consolidation treatment options include:
  - Bladder removal surgery (radical cystectomy)
  - Chemoradiation therapy

If some cancer is found after chemotherapy, then you can have additional treatment to try a different strategy. Additional treatment options include:

- Radical cystectomy (for cancer in the bladder only)
- Chemoradiation therapy (for persistent cancer in the bladder)
- Treatment for metastatic disease (for cancer located outside the bladder)

If the cancer continues to grow or spread despite chemotherapy, then the next step is to begin treatment for metastatic disease. See Chapter 7.

Follow-up

For recommendations on follow-up care and monitoring for the return of cancer, see page 58.

Chemoradiation

The other main treatment option for stage 3B bladder cancer is chemoradiation therapy—a combination of chemotherapy and radiation therapy. When given together, both treatments work better than either does alone.

About 2 to 3 months after you've finished chemoradiation, you'll have imaging tests to see how well the treatment worked.

If no cancer is found after chemoradiation, no further treatment is needed. You can begin follow-up care and monitoring for cancer recurrence.

If some cancer is found after chemoradiation, then you can have additional treatment to try a different strategy. Options for additional treatment include:

- Intravesical BCG therapy (if the tumor shrank enough so that it no longer invades the muscle wall of the bladder)
- Radical cystectomy (for cancer in the bladder only)
- Treatment for metastatic disease (for cancer located outside the bladder)

If the cancer continues to grow or spread even after chemoradiation, then the next step is to

begin treatment for metastatic disease. See Chapter 7.

Follow-up

For recommendations on follow-up care and monitoring for the return of cancer, see page 58.

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 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 spread to the far away lymph nodes. Stage 4A bladder cancer that **has** spread to distant lymph nodes is considered metastatic. 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, you may be treated with one of these main options:

- Combination chemotherapy with cisplatin-based medicine. If you can't have cisplatin, other chemotherapy, immunotherapy, and targeted therapy medicines are available for stage 4A cancer. For recommended systemic therapy options, **see Guide 8.**
- Chemoradiation therapy. This is a combination of chemotherapy and radiation therapy. When given together, both treatments work better than either does alone.

After either treatment, you'll need a few tests to see if the therapy worked. Tests include cystoscopy, TURBT, and imaging of your abdomen and pelvis. Testing is recommended after 2 to 3 cycles of chemotherapy, or 2 to 3 months after finishing chemoradiation.

If the tests show that the cancer didn't grow or spread after either platinum-based chemotherapy or chemoradiation, you can have maintenance treatment to retain the benefits of therapy and to slow the cancer from growing. Bavencio (avelumab), a checkpoint inhibitor, is the preferred maintenance option.

If no cancer is found after initial therapy, additional treatment options may also help the cancer from coming back. These include:

- Systemic therapy to wipe out any undetectable cancer cells that may have been left behind. Systemic therapy options include targeted therapy or chemotherapy.
- Chemoradiation 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 help get rid of more of the cancer. Additional treatment options include:

- Systemic therapy with either targeted therapy or chemotherapy. For treatment options, **see Guide 9.**
- Chemoradiation therapy (if you haven't had radiation therapy before).

Guide 9
Next treatment options for stage 4A bladder cancer

What other treatment did you have before?	Next preferred options	Other recommended options

Platinum-based chemotherapy or other chemotherapy	• Keytruda (pembrolizumab)
	• Other treatment options:
	  • Opdivo (nivolumab)
	  • Bavencio (avelumab)
	  • Balversa (erdafitinib)
	  • Padcev (enfortumab vedotin-ejfv)
		• Taxol (paclitaxel)
		• docetaxel
		• gemcitabine

Checkpoint inhibitor* and you're able to have cisplatin	• gemcitabine and cisplatin • dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin (ddMVAC)	• ifosfamide, doxorubicin, and gemcitabine • gemcitabine and Taxol (paclitaxel)
Checkpoint inhibitor* but you're not able to have cisplatin	• Padcev (enfortumab vedotin-ejfv) • gemcitabine and carboplatin	• Balversa (erdafitinib) • Taxol (paclitaxel) • docetaxel • gemcitabine
Additional treatment options after having treatment above:		
Platinum-based chemotherapy and checkpoint inhibitor*	• Padcev (enfortumab vedotin-ejfv) • Balversa (erdafitinib) – *only if you have* FGFR2 *or* FGFR3 *genetic mutation*	• Trodelvy (sacituzumab govitecan-hziy) • gemcitabine • Taxol (paclitaxel) • docetaxel • ifosfamide, doxorubicin, and gemcitabine • gemcitabine and Taxol (paclitaxel) • gemcitabine and cisplatin • ddMVAC

** Checkpoint inhibitors include Bavencio, Keytruda, Opdivo, and Tecentriq.*

- Radical cystectomy (if the main treatment shrank the tumor enough).

Follow-up

For recommendations on follow-up care and monitoring for cancer recurrence, see page 58.

Stage 4A metastatic

If stage 4A cancer has spread to distant lymph nodes in your body (metastasized), the main treatment is systemic therapy. Systemic therapy is treatment that affects cancer cells throughout the whole body. For recommended systemic therapy options, **see Guide 8.**

After treatment, you'll have a few tests to see if the therapy worked. Tests include cystoscopy, TURBT, and imaging of your abdomen and pelvis.

Guide 10
Follow-up tests after bladder removal 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">At 3 and 12 months:
• Urogram (CT or MRI)
• Chest CT or chest x-ray</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</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</td><td rowspan="4">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</td></tr>
<tr><td>After 10 years</td><td>As directed by your doctor</td></tr>
</table>

If the tests show that the cancer didn't grow or spread after either platinum-based chemotherapy or chemoradiation, you may have maintenance treatment to retain the benefits of therapy and to slow the cancer from growing. Bavencio (avelumab), a checkpoint inhibitor, is the preferred maintenance option.

If no cancer is found or if there's less cancer after initial therapy, then your doctor may ask you to consider local therapy with 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 who had good results with systemic therapy.

If the cancer stays the same or if it continues to grow, your next step is treatment for metastatic disease. See Chapter 7. You can also consider joining a clinical trial.

Follow-up care

When you've finished initial 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 book, bladder cancer can come back at any time. So be sure you don't skip or forget to go to 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 removed.

If your bladder was removed

Even if you had surgery to remove your bladder, cancer can still 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 radical cystectomy, **see Guide 10.** Keep in mind that every person's follow-up plan will be 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 recommended during the first 2 years of follow-up care for people who have a high risk of cancer recurrence.

People who have 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 you have your bladder

For those who were able to keep their bladder, there's always a risk that cancer will return to the bladder, to another part of the urinary tract, or to 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 11.** Keep in mind that every person's follow-up plan will be different.

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 work, it's helpful to know how to deal with it. Treatment for recurrent

Guide 11
Follow-up tests after bladder preserving treatment for muscle-invasive bladder cancer

	Cystoscopy	Imaging	Blood tests	Urine tests
Year 1	**Every 3 months**	**At 3 and 12 months:** • Urogram (CT or MRI) • Chest CT or chest x-ray	**Every 3–6 months:** • Kidney function • Liver function • CBC and CMP (if you had chemotherapy)	**Every 6–12 months:** • Uterine cytology • Urethral wash cytology (only if high risk of recurrence)
Year 2				
Year 3	**Every 6 months**	**Once a year:** • CT or MRI of abdomen and pelvis • Chest CT or chest x-ray	**Once a year:** • Kidney function • Liver function • B12 level	**As directed by your doctor:** • Urine cytology • Urethral wash cytology (only if high risk of recurrence)
Year 4				
Year 5	**Once a year**			
Years 6–10		**Once a year:** • Ultrasound of the kidneys	**Once a year:** • B12 level	
After 10 years	**As directed by your doctor**	**As directed by your doctor**		

or persistent muscle-invasive bladder cancer is based on the results of follow-up tests and whether your bladder was removed.

If you have your bladder

If cancer is found in a person with a preserved bladder, 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 recurrent cancer in the bladder, but not in other areas of the body, it should be treated like it's a new cancer. Treatment depends on whether or not it has invaded the muscle wall.

- **Not invaded the muscle wall** – These tumors are usually treated with intravesical BCG therapy or a radical cystectomy.
- **Invaded the muscle wall** – These tumors are usually treated with a radical cystectomy. Chemoradiation is also an option if you've never been treated with radiation therapy before. If you can't have cystectomy or chemoradiation, other options are chemotherapy or TURBT for pain relief, as well as supportive care to treat any symptoms.

Cancer in another part of the urinary tract

If urine cytology tests indicate cancer 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 also be very serious.

- **Cancer in the ureters or kidneys** – To check the upper urinary tract, fluid is put into the ureters and kidneys. The fluid is then removed and tested for cancer cells. 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.

If your bladder was removed

If your bladder was removed, but recurrent cancer is found in the bladder area or in areas outside the bladder (metastasis), you have several treatment options. These may include chemotherapy or other systemic therapy, chemoradiation therapy (if you haven't had radiation therapy before), or radiation therapy alone.

Next steps

After you've been treated for recurrent or persistent cancer, you'll continue to have tests and visits every so often to watch out for the cancer to return or progress. Surveillance is a key part of the follow-up plan. Just know that you can have bladder cancer and still lead a fulfilling life after diagnosis and treatment.

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

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 cancers are muscle-invasive.
- Radical cystectomy is the main treatment for people with stage 2 or 3A bladder cancer who are healthy enough for surgery. Cisplatin-based chemotherapy is often given beforehand to shrink the tumor prior to the surgery.
- Some people with stage 2 or 3A muscle-invasive bladder cancer can't have or don't want a radical cystectomy. For these people, treatment options include TURBT and chemoradiation, radiation therapy alone, or TURBT alone.
- The main treatment options for stage 3B and 4A bladder cancers are systemic therapy or chemoradiation.
- 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.

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

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.

7

Treatment for metastatic bladder cancer

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.

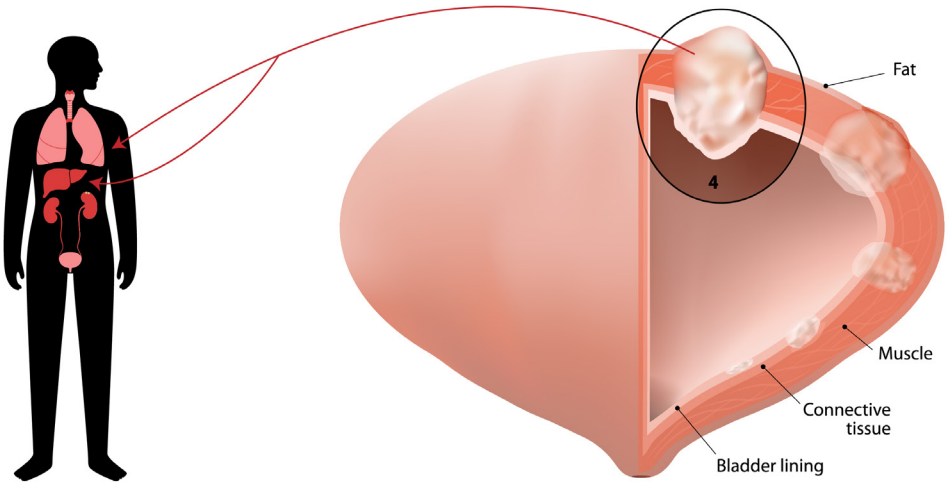
Stage 4B is metastatic bladder cancer. This cancer has grown through the bladder wall and has spread (metastasized) to lymph nodes or organs far from the bladder. Metastatic bladder cancer may have spread to areas like the bones, liver, or lungs.

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, especially 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 these and other resources.

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.



Tests to plan treatment

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

The main treatment for metastatic bladder cancer is usually systemic therapy. Systemic therapies—like chemotherapy, immunotherapy,

Guide 12
First-line treatment options for stage 4B bladder cancer

Can you have cisplatin?	Systemic treatment options	Drug type	Maintenance therapy afterward
Yes, I can have cisplatin	Gemcitabine and cisplatin*	Chemotherapy	Bavencio (avelumab) immunotherapy
	Dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin (ddMVAC)*	Chemotherapy	Bavencio (avelumab) immunotherapy
No, I can't have cisplatin	Gemcitabine and carboplatin*	Chemotherapy	Bavencio (avelumab) immunotherapy
	Keytruda (pembrolizumab)*	Immunotherapy	none
	Padcev (enfortumab vedotin-ejfv) and Keytruda (pembrolizumab)*	Targeted therapy and immunotherapy	none
	Gemcitabine	Chemotherapy	none
	Gemcitabine and Taxol (paclitaxel)	Chemotherapy	none
	Tecentriq (atezolizumab) - *only if your cancer has PD-L1 biomarker*	Immunotherapy	none
	Ifosfamide, doxorubicin, and gemcitabine – only if you have good kidney function and good activity level	Chemotherapy	none

** Preferred options.*

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 your ability to do day-to-day activities.

Tests may include:

- Bone scan 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
- Molecular or genomic testing to find biomarkers that show you can have certain targeted therapies.

First therapy

NCCN experts recommend starting with one of the systemic therapy options in **Guide 12.** These are called “first-line” therapies because they have the best chance of working, so they should be used first.

Many patients with bladder cancer can have a good response to chemotherapy. So chemotherapy is often the first treatment used. Which specific chemotherapy to use depends in part on whether you have other diseases or conditions, and whether your body can handle difficult treatment.

If you can handle cisplatin-based chemotherapy, then your first-line treatment may be either gemcitabine and cisplatin or a combination of methotrexate, vinblastine, doxorubicin, and cisplatin (known as ddMVAC).

If your body can’t handle cisplatin but can tolerate carboplatin, then your first-line treatment may be gemcitabine and carboplatin.

If your body can’t tolerate any platinum-based chemotherapy, then an immunotherapy treatment may be your best option. The preferred first-line immunotherapy is Keytruda (pembrolizumab), a checkpoint inhibitor.

Other first-line treatments may be useful in certain situations, depending on the therapy you’ve already received. A relatively new option is targeted therapy with Padcev (enfortumab vedotin-ejfv) plus Keytruda.

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.

Maintenance therapy

If your cancer didn't grow or spread after having first-line platinum-based chemotherapy, then you may have maintenance treatment to retain the benefits of therapy and to slow the cancer from growing. Bavencio (avelumab), a checkpoint inhibitor, is the preferred maintenance option.

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. Because this type of radiation doesn’t aim to cure the cancer, lower doses can be used,

which lessens the side effects of the therapy. Ask your treatment team if you're able to have this kind of radiation.

Follow-up

After 2 to 3 cycles of chemotherapy treatment, your treatment team will want to see how well the therapy is working. Follow-up tests are listed in **Guide 13.**

If the cancer stays the same or improves, treatment is usually continued for 2 more cycles.

If the cancer continues to grow or if the chemotherapy is too harsh, a different treatment should be considered. In most cases, you shouldn't have more than 6 cycles of chemotherapy.

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 14.** Next treatment options depend on which first-line therapy you were treated with.

If you had chemotherapy as your first-line treatment, then the preferred next treatment option is immunotherapy with Keytruda, a checkpoint inhibitor. Other preferred next treatment options include Opdivo (nivolumab), Bavencio, Padcev (enfortumab vedotin-ejfv), or Balversa (if molecular testing shows you have changes in either *FGFR2* or *FGFR3* genes).

If you had platinum-based chemotherapy (cisplatin or carboplatin) more than 12 months ago, you may be able to have it again if your body can tolerate it.

If your first-line therapy was a checkpoint inhibitor (such as Keytruda, Bavencio, Opdivo, or Tecentriq), then the preferred next treatment option depends on whether you're able to have cisplatin-based chemotherapy. If you can have it, then your options include gemcitabine and cisplatin or a combination of methotrexate, vinblastine, doxorubicin, and cisplatin (ddMVAC). If you're not able to

Guide 13
Follow-up tests after first-line treatment for metastatic bladder cancer

	Cystoscopy	Imaging	Blood tests	Urine tests
Test frequency	**As directed by your doctor**	**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	**Every 1–3 months:** • CBC and CMP **Once a year:** • B12 level if you had a cystectomy	**As directed by your doctor:** • Urine cytology

Guide 14
Next treatment options for stage 4B bladder cancer

What other treatment did you have before?	Next preferred options	Other recommended options

Platinum-based chemotherapy or other chemotherapy	• Keytruda (pembrolizumab)
	• Other treatment options:
	  • Opdivo (nivolumab)
	  • Bavencio (avelumab)
	  • Balversa (erdafitinib)
	  • Padcev (enfortumab vedotin-ejfv)
		• Taxol (paclitaxel)
		• docetaxel
		• gemcitabine

Checkpoint inhibitor* and you're able to have cisplatin	• gemcitabine and cisplatin • dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin (ddMVAC)	• ifosfamide, doxorubicin, and gemcitabine • gemcitabine and Taxol (paclitaxel)
Checkpoint inhibitor* but you're not able to have cisplatin	• Padcev (enfortumab vedotin-ejfv) • gemcitabine and carboplatin	• Balversa (erdafitinib) • Taxol (paclitaxel) • docetaxel • gemcitabine
Additional treatment options after having treatment above:		
Platinum-based chemotherapy and checkpoint inhibitor*	• Padcev (enfortumab vedotin-ejfv) • Balversa (erdafitinib) – *only if you have* FGFR2 *or* FGFR3 *genetic mutation*	• Trodelvy (sacituzumab govitecan-hziy) • gemcitabine • Taxol (paclitaxel) • docetaxel • ifosfamide, doxorubicin, and gemcitabine • gemcitabine and Taxol (paclitaxel) • gemcitabine and cisplatin • ddMVAC

** Checkpoint inhibitors include Bavencio, Keytruda, Opdivo, and Tecentriq.*

have cisplatin-based chemotherapy, then your options include Padcev or gemcitabine and carboplatin.

Other treatments not listed in Guide 14 may be useful in certain situations, depending on the treatment you've already received.

After you've had treatment with both platinum-based chemotherapy and a checkpoint inhibitor, the next preferred treatment option is Padcev. For people who have genetic changes in either the *FGFR2* or *FGFR3* gene, Balversa is also an option. Other possible options include the targeted therapy Trodelvy (sacituzumab govitecan-hziy) or various chemotherapy treatments.

Other treatments

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 lung, for example)

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.

Now what?

After you've been treated for metastatic bladder cancer, you'll continue to have tests and visits to watch out 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 continue to go to follow-up visits and stay in touch with your treatment 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 at times like there's no 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.

For information about supportive care and other assistance, turn to Chapter 8.

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.
- You should 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 (checkpoint inhibitors), 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 pain or discomfort from bladder cancer.
- Supportive care aims to improve your quality of life. It includes care for cancer symptoms, side effects caused by cancer treatment, and other issues related to cancer.

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

8

Supportive care and other assistance

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 to your questions.

The main concern for most patients with cancer is to find treatment that works. Having cancer is about more than treatment, though. Cancer care is a rollercoaster that includes many additional physical and emotional challenges. It's important to know that you can get support for these challenges.

Supportive care

Supportive care is for relieving the symptoms of cancer and the side effects of cancer therapies, and other health issues related to the cancer. Supportive care also helps with psychological, social, and spiritual issues. Supportive care involves the whole person, not just their cancer.

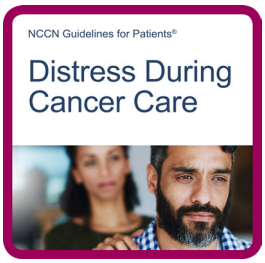
Supportive care is given at any stage of disease, not just at the end of life.

Supportive care addresses many needs. It can help with making treatment decisions. It can also assist with coordinating care between health providers. Notably, supportive care can help prevent or treat physical and emotional symptoms. Supportive care can also help with financial support, advance care planning, and end-of-life concerns.

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.



It's important to talk openly with your treatment team about supportive care. Ask questions and reach out if you need more information about your next steps.

Anxiety and depression

Many people with cancer experience 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 that you can get help.

Help can include support groups, talk therapy, or medication. At your cancer center, cancer navigators, social workers, and other experts can help. Some people also feel better by exercising, talking with 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 84 of this book.

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 can help you find financial support and transportation options.

Financial resources

American Cancer Society (cancer.org/treatment/finding-and-paying-for-treatment.html) has general information about financial and insurance issues of cancer.

American Society of Clinical Oncology (cancer.net/navigating-cancer-care/financial-considerations) offers information about financial considerations and dealing with the costs of cancer care.

HealthWell Foundation (healthwellfoundation.org) provides financial assistance to people with cancer or other chronic diseases who are underinsured.

National Cancer Institute (cancer.gov/about-cancer/managing-care/track-care-costs) has tips about managing the cancer costs.

Patient Advocate Foundation (patientadvocate.org) provides case management services and financial aid to people with cancer or other severe illnesses.

Triage Cancer (triagecancer.org) offers free education on practical and legal issues for people with cancer.

You can also talk to your treatment team about work, insurance, or money problems. They'll include information in the treatment plan to help you manage your finances and medical costs. If your doctors and care providers 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 keeps progressing 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 cancers are curable, talking about future scenarios should begin when starting treatment.

Advance care planning means deciding what care you would want if you become unable to make medical decisions for yourself. It's about making sure that your wishes are understood and respected. The focus is on you receiving the best possible care at the end of your life. Patients with incurable cancer can set up an advance care plan early on to feel less stressed and better able to cope with their condition.

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.

Exercise can make you feel better. Plus, research has shown that exercise helps some people with bladder cancer live longer.

This discussion should include your spouse or partner and other family members who love you and 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 is 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 of your advance directive to all your doctors. Make sure you give a copy to anyone

you've authorized to make decisions on your behalf (health care proxy). 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 the people who love them. The goal is comfort, not a 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.

Key points

- Supportive care is for relieving symptoms, side effects, and other health issues related to cancer.
- Know that you can also get support for psychological, social, and spiritual issues.
- Supportive care is treatment that involves the whole person, not just their cancer.
- Supportive care is given at any stage of disease, not just at 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.
- An advance directive is a legal document that explains your care if you're too ill to give instructions about it yourself.
- Hospice care is for people who are close to the end of life. It's focused on comfort and quality of life.
- A key part of hospice care is providing support to family members.

9
Making treatment decisions

It's important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your care team.

It's your choice

Treatment decisions are very personal. What's important to you may not be important to someone else.

In shared decision-making, you and your care team share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your team.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments like surgery or chemotherapy
- Your feelings about pain or side effects
- Cost of treatment, travel to treatment centers, and time away from school or work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your care team. If you can build a relationship with your team, you'll feel supported when considering options and making treatment decisions.

Second opinion

It's normal to want to start treatment as soon as possible. While cancer treatment shouldn't be ignored, there is usually time to have another cancer care provider review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Seek out a bladder cancer specialist, if you can, because they have experience diagnosing and treating a lot of people with bladder cancer.

Things you can do to prepare for a second opinion:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your second opinion.

Questions to ask

Possible questions to ask your cancer care team are listed on the following pages. Feel free to use these or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment. Have a notebook handy to jot down the answers to your questions.

Questions about cancer testing

1. What tests will I have? How do I prepare for testing?
2. Do the tests have any risks?
3. Where do I go for testing, and how long will it take?
4. Will any of the tests hurt?
5. How often are these tests wrong?
6. Should I bring someone with me to my appointments?
7. How soon will I know the results and who will explain them to me?
8. How can I get a copy of the pathology report and other test results?
9. Who will talk to me about the next steps?

Questions about treatment options

1. Can my type of bladder cancer be cured? If not, how well can treatment stop it from growing?
2. What are my treatment options?
3. Are you suggesting treatment options from the NCCN Guidelines, or have you modified the standard treatment in my situation?
4. Does this hospital/center offer the best treatment for me?
5. How do my age, sex, overall health, and other factors affect my options? What impact would quitting smoking have on my results?
6. Are my chances any better for one option than another?
7. What will happen if I do nothing?
8. How do I get a second opinion?
9. How long do I have to decide about treatment? Is there a social worker or someone who can help me decide?
10. Do I have a choice of when to begin treatment?

Questions about getting treatment

1. Where will I receive treatment—in a hospital, a clinic, your office, or at home?
2. How long will the treatment last?
3. Will the treatment hurt?
4. What supportive care and services are available to me and my caregivers?
5. Who should I contact with questions or concerns if the office is closed?
6. How will you know if treatment is working? What are my options if treatment stops working?
7. What are the chances of the cancer worsening or returning?
8. What follow-up care is needed after treatment?
9. Will I be able to return to my normal activities? If so, when?

Questions about side effects

1. What are the possible complications and side effects of treatment?
2. Does the cancer itself cause any side effects?
3. Which side effects are most common and how long do they usually last?
4. Are there any long-term or permanent side effects?
5. Are there any side effects that are serious or life-threatening?
6. What symptoms should I report right away, and who do I contact?
7. What can be done to prevent or relieve the side effects of treatment?
8. What can be done to preserve my sexual function?
9. Do any side effects lessen or worsen in severity over time?
10. Will you stop or change treatment if there are serious side effects?

Questions about clinical trials

1. Are there clinical trial options for me?
2. How do I find clinical trials that I can participate in?
3. What are the treatments used in the clinical trial?
4. Has the treatment been used for other types of cancer?
5. What are the risks and benefits of this treatment?
6. What side effects should I expect and how will they be managed?
7. How long will I be in the clinical trial?
8. Will I be able to get other treatment if this doesn't work?
9. How will you know if the treatment is working?
10. Will the clinical trial cost me anything?

Questions about your care team’s experience

1. Are you board certified? If yes, in what area?
2. What is your experience as well as your team's experience with treating the type of cancer I have?
3. How many patients like me (of the same age, gender, race) have you treated?
4. Will you be consulting with experts to discuss my care? Whom will you consult?
5. Is this treatment (or procedure) a major part of your practice? How often have you done this treatment (or procedure) in the last year?
6. How many of your patients have had complications? What were the complications?

Questions about affording care

1. Will my insurance pay for all the tests you're recommending?
2. Will my insurance cover the treatments you're recommending? How much will I have to pay myself?
3. Is there another treatment that will work as well but cost less?
4. Are there any grants or programs to help pay for testing or treatment?
5. Does my insurance plan require preapproval before I start treatment?
6. Who can I talk to about financial help or payment options?

Resources

American Bladder Cancer Society
bladdercancersupport.org

American Society of Clinical Oncology
cancer.net/cancer-types/bladder-cancer

Bladder Cancer Advocacy Network
bcan.org

Cancer*Care*
cancercare.org

Cancer Hope Network
cancerhopenetwork.org

National Cancer Institute
cancer.gov/types/bladder

Triage Cancer
triagecancer.org

United Ostomy Associations of America
ostomy.org

Urology Care Foundation
urologyhealth.org

Words to know

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

biomarker
Something found in your body that can be measured to assess your health. Usually identified by a blood test or a test of tumor tissue.

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

bone scan
An imaging test used to view bones for cancer or other problems.

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. Chemotherapy for bladder cancer can be given as systemic or intravesical therapy.

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

consolidation therapy
A treatment given after the initial therapy kills all visible cancer. Consolidation therapy is used to treat any cancer cells left behind by previous therapy.

continent urinary reservoir
A type of urinary diversion in which a portion of the large intestine is used as a pouch to hold urine. A section of the small intestine connects the pouch to a hole (stoma) in the wall of the abdomen. A catheter is used to drain urine from the reservoir. Also called an Indiana pouch.

cystectomy
A surgical procedure that removes all or part of the bladder.

cystoscopy
A procedure that allows a doctor 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.

external beam radiation therapy (EBRT)
A cancer treatment in which a machine outside the body sends radiation to cancer cells inside the body.

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
A type of 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
A drug treatment that helps the body's immune system find and destroy cancer cells.

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

local therapy
A treatment given to a specific area or organ of the body. Examples are surgery and radiation.

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

mutation
An abnormal change in the genetic instructions for making and controlling cells.

neobladder
A type of urinary diversion in which a piece of small intestine is made into a new urinary reservoir. This is connected directly to the urethra so you can pee more normally.

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

positron emission tomography (PET)
A test that uses radioactive material to see the shape and function of body parts.

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

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

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

resection
A surgical procedure 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.

supportive care
Health care that relieves symptoms caused by cancer or by its treatment.

surveillance
Ongoing testing after treatment ends to watch for cancer to return.

systemic therapy
A type of treatment that works throughout the body.

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

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

trimodal therapy
A combination of three therapies—TURBT, chemotherapy, and radiation therapy—used to preserve the bladder in certain people with muscle-invasive bladder cancer.

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
A type of 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 inside of the urinary tract.

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

variant
In bladder cancer, a subtype of urothelial cell cancer that also has features of another, less common cell type.

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer, Version 2.2023. It was adapted, reviewed, and published with help from the following people:

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Abramson Cancer Center
at the University of Pennsylvania
Philadelphia, Pennsylvania
800.789.7366 • pennmedicine.org/cancer

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer Center and
Cleveland Clinic Taussig Cancer Institute
Cleveland, Ohio
UH Seidman Cancer Center
800.641.2422 • uhhospitals.org/services/cancer-services
CC Taussig Cancer Institute
866.223.8100 • my.clevelandclinic.org/departments/cancer
Case CCC
216.844.8797 • case.edu/cancer

City of Hope National Medical Center
Duarte, California
800.826.4673 • cityofhope.org

Dana-Farber/Brigham and Women's Cancer Center |
Massachusetts General Hospital Cancer Center
Boston, Massachusetts
617.732.5500 • youhaveus.org
617.726.5130 • massgeneral.org/cancer-center

Duke Cancer Institute
Durham, North Carolina
888.275.3853 • dukecancerinstitute.org

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427 • foxchase.org

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
402.559.5600 • unmc.edu/cancercenter

Fred Hutchinson Cancer Center
Seattle, Washington
206.667.5000 • fredhutch.org

Huntsman Cancer Institute at the University of Utah
Salt Lake City, Utah
800.824.2073 • huntsmancancer.org

Indiana University Melvin and Bren Simon
Comprehensive Cancer Center
Indianapolis, Indiana
888.600.4822 • www.cancer.iu.edu

Mayo Clinic Comprehensive Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
480.301.8000 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
mayoclinic.org/cancercenter

Memorial Sloan Kettering Cancer Center
New York, New York
800.525.2225 • mskcc.org

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • moffitt.org

O'Neal Comprehensive Cancer Center at UAB
Birmingham, Alabama
800.822.0933 • uab.edu/onealcancercenter

Robert H. Lurie Comprehensive Cancer
Center of Northwestern University
Chicago, Illinois
866.587.4322 • cancer.northwestern.edu

Roswell Park Comprehensive Cancer Center
Buffalo, New York
877.275.7724 • roswellpark.org

Siteman Cancer Center at Barnes-Jewish Hospital
and Washington University School of Medicine
St. Louis, Missouri
800.600.3606 • siteman.wustl.edu

St. Jude Children's Research Hospital/
The University of Tennessee Health Science Center
Memphis, Tennessee
866.278.5833 • stjude.org
901.448.5500 • uthsc.edu

Stanford Cancer Institute
Stanford, California
877.668.7535 • cancer.stanford.edu

The Ohio State University Comprehensive Cancer Center -
James Cancer Hospital and Solove Research Institute
Columbus, Ohio
800.293.5066 • cancer.osu.edu

The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins
Baltimore, Maryland
410.955.8964
www.hopkinskimmelcancercenter.org

The UChicago Medicine Comprehensive Cancer Center
Chicago, Illinois
773.702.1000 • uchicagomedicine.org/cancer

The University of Texas MD Anderson Cancer Center
Houston, Texas
844.269.5922 • mdanderson.org

UC Davis Comprehensive Cancer Center
Sacramento, California
916.734.5959 • 800.770.9261
health.ucdavis.edu/cancer

UC San Diego Moores Cancer Center
La Jolla, California
858.822.6100 • cancer.ucsd.edu

UCLA Jonsson Comprehensive Cancer Center
Los Angeles, California
310.825.5268 • cancer.ucla.edu

UCSF Helen Diller Family
Comprehensive Cancer Center
San Francisco, California
800.689.8273 • cancer.ucsf.edu

University of Colorado Cancer Center
Aurora, Colorado
720.848.0300 • coloradocancercenter.org

University of Michigan Rogel Cancer Center
Ann Arbor, Michigan
800.865.1125 • rogelcancercenter.org

University of Wisconsin Carbone Cancer Center
Madison, Wisconsin
608.265.1700 • uwhealth.org/cancer

UT Southwestern Simmons
Comprehensive Cancer Center
Dallas, Texas
214.648.3111 • utsouthwestern.edu/simmons

Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
877.936.8422 • vicc.org

Yale Cancer Center/Smilow Cancer Hospital
New Haven, Connecticut
855.4.SMILOW • yalecancercenter.org

Notes

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