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Bladder Cancer

Urothelial Carcinoma

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American Bladder Cancer Society

We believe in support, the power of knowledge, and hope. A diagnosis of cancer is a frightening thing. Patients and their families need multiple sources of accurate and realistic information. The American Bladder Cancer Society endorses the presence of sites such as NCCN which will reach many individuals seeking answers. It is also urgent that people are made aware of the signs and symptoms of cancers, including bladder cancer, because early diagnosis and treatment can be life-saving. <https://bladdercancersupport.org>

Bladder Cancer Advocacy Network

As the largest bladder cancer advocacy organization in the world, BCAN is proud to endorse the NCCN Guidelines for Patients®: Bladder Cancer. These important guidelines, grounded in clinical practice, help those diagnosed with bladder cancer to speak confidently with their provider about the best treatment options to manage their bladder cancer diagnosis. www.bcan.org

Urology Care Foundation

The Urology Care Foundation is the world's leading nonprofit urological health foundation – and the official foundation of the American Urological Association. As an organization who strongly believes in providing patients, caregivers and those impacted by bladder cancer educational tools and resources to make informed decisions about their health and treatment, we are pleased to endorse the NCCN Guidelines for Patients®: Bladder Cancer.

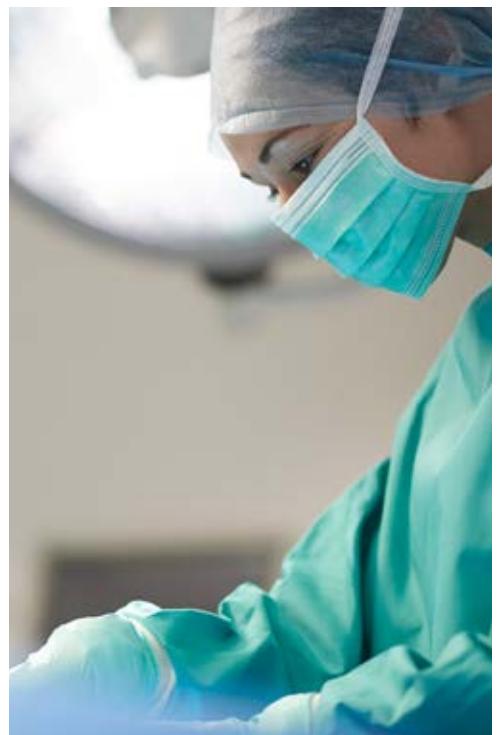
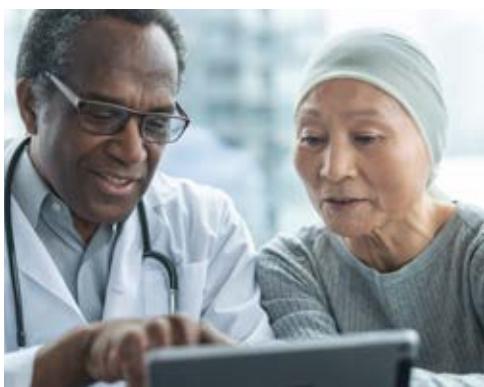
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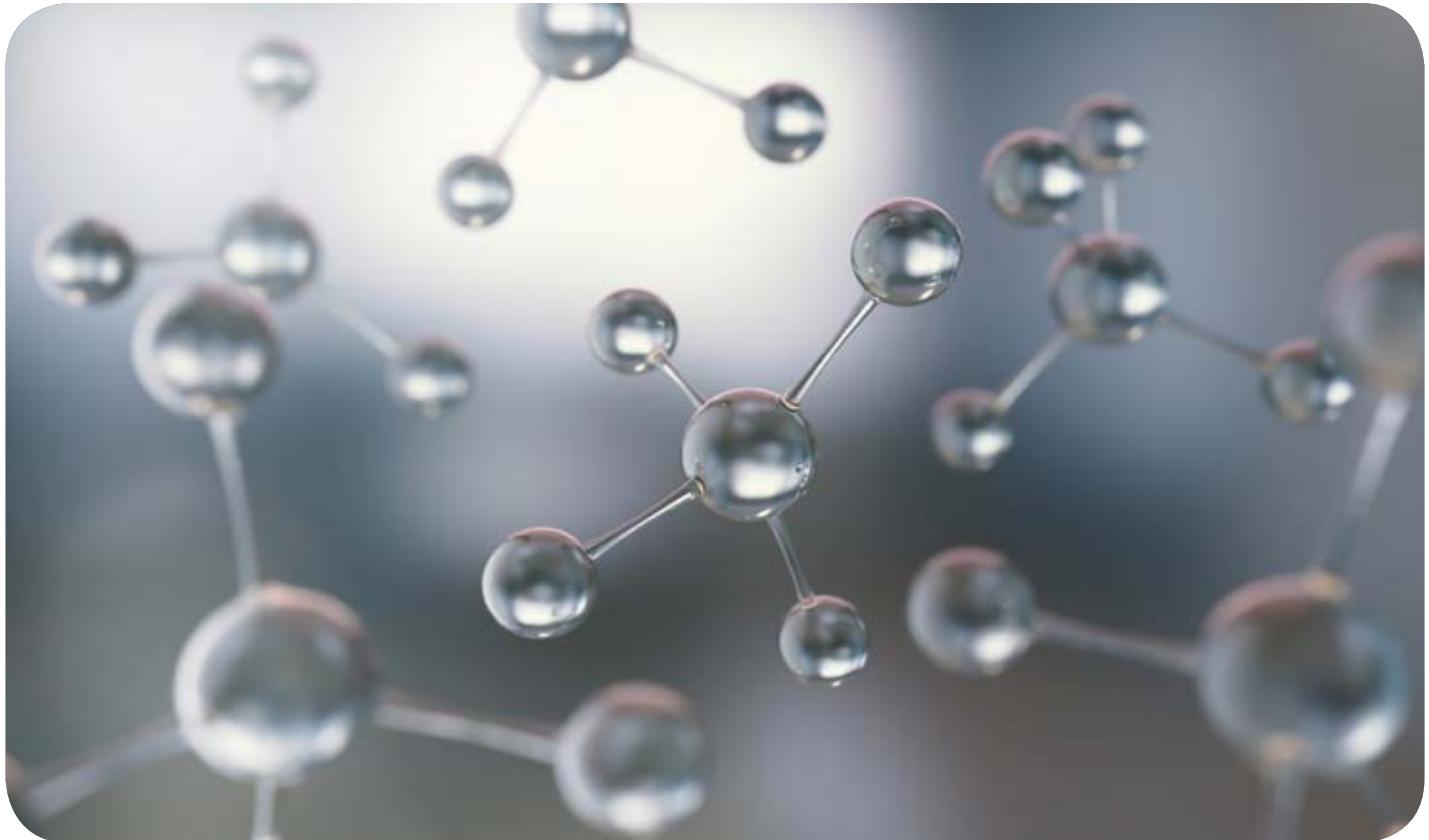
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Bladder cancer basics

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This chapter provides some basic information about cancer and how it affects the bladder. This introduction to bladder cancer will help prepare you for treatment.

The urinary system

The bladder is a hollow organ with a thick muscular layer that plays an important role in the urinary system. **See Figure 1**. The other organs in the urinary system are the kidneys, ureters, and urethra. Urine is made in the kidneys and then travels down two tubes called ureters to the bladder. The bladder expands to accommodate the urine and stores it until you are ready to urinate (pee). Urine then leaves the bladder and travels out of the body through a tube called the urethra. **See Figure 2**.

In order to understand how bladder cancer starts and spreads, it is helpful to have some basic information

about the structure of the bladder. The outside of the bladder (the bladder wall) is made of layers that have different functions.

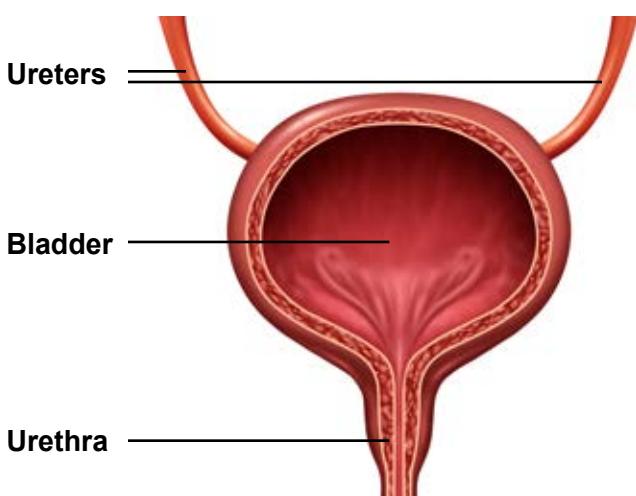
The innermost layer, or lining, of the bladder is called the urothelium. The urothelium is made of cells called urothelial cells. Urothelial cells are unique because they can stretch without breaking. They allow the bladder and other hollow organs of the urinary system to expand to hold urine.

After the urothelium, the next layer of the bladder wall is made of connective tissue. This layer is called the lamina propria. The next part of the bladder wall is made of muscle. This layer is called the detrusor muscle, or the muscularis propria. The detrusor muscle stays relaxed to allow urine to fill the bladder, and then contracts to allow urine to leave the body during urination.

A fatty layer surrounds the detrusor muscle. This outermost layer of fat that surrounds the bladder is called the adventitia or serosa.

Figure 1. The bladder

The bladder is a hollow organ in the urinary tract that expands to hold urine, much like a balloon.



Types of bladder cancer

Histology is the study of tissues and cells under a microscope. In order to diagnose bladder cancer, a piece of tissue is removed from the suspicious area of the bladder for testing (a biopsy). A pathologist is an expert in studying cells and tissues under a microscope. He or she determines the specific type of bladder cancer based on the type and appearance of the cells.

Urothelial carcinomas of the bladder

The inside lining of the bladder is called the urothelium, which is made of urothelial (also called transitional) cells. **Most bladder cancers start in urothelial cells.** When bladder cancer starts

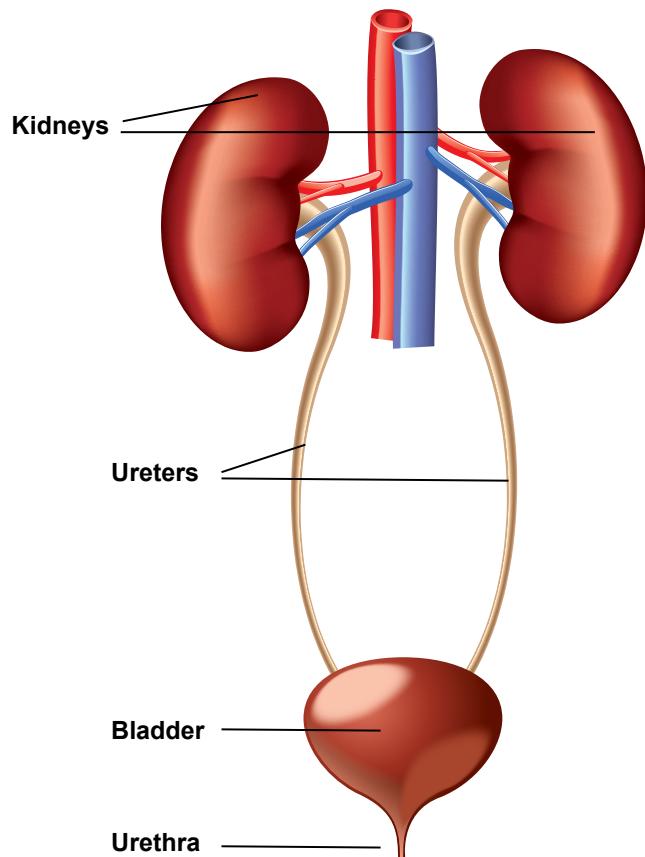
in urothelial cells, it is called urothelial carcinoma (formerly called transitional cell carcinoma).

Most people have what's called "pure" urothelial carcinoma. This means that, when viewed under a microscope, all of the cells fit the "classic" description of urothelial carcinoma used by scientists.

Sometimes bladder cancer cells don't have the typical appearance of traditional urothelial cells. These cancers are called "variant histologies" of urothelial carcinoma. Bladder tumors can also be made of two different types of cells (urothelial and a different type of cell also found in the urinary tract). These cancers are called "mixed histologies" of urothelial carcinoma.

Figure 2. The urinary tract

The kidneys and ureters are often referred to as the "upper urinary tract."
The bladder and urethra are commonly known as the "lower urinary tract."



It is important to know whether your cancer is a variant of urothelial carcinoma because it can affect treatment planning. For example, some variant histologies are very fast-growing and so require more aggressive treatment, or a different type of treatment. Some of the variant histologies of urothelial carcinoma are listed below for your reference.

Please note that this book only discusses treatment of pure urothelial carcinoma.

- Urothelial carcinoma mixed with any of these other types of cells found in the urinary system:
 - Squamous (pronounced *skway-miss*) cells
 - Glandular cells (examples include adenocarcinoma and villous adenoma)
 - Trophoblastic cells (very rare)
- Micropapillary
- Nested, including large nested
- Microcystic
- Lymphoepithelioma-like
- Plasmacytoid
- Sarcomatoid
- Poorly differentiated
- Lipid-rich (very rare)
- Clear cell

Non-urothelial carcinomas of the bladder

While rare, bladder cancer can start in a cell other than a urothelial (transitional) cell. These much less common types of bladder cancer are listed below for your information. This book does not address treatment of these rare types of bladder cancer.

- Squamous cell carcinoma
- Adenocarcinoma
- Small cell carcinoma



SNAPSHOT

Bladder cancer

- ✓ The 6th most common type of cancer in the United States
- ✓ More common in men than women
- ✓ Most people diagnosed in their 70's
- ✓ Blood in the urine is the most common symptom
- ✓ The most common type of bladder cancer is called "urothelial carcinoma" (formerly known as "transitional cell carcinoma")
- ✓ Women and African-Americans tend to be diagnosed later and have worse outcomes

- Sarcoma (see the *NCCN Guidelines for Patients®: Soft Tissue Sarcoma*)

Other cancers of the urinary system

While much less common than bladder cancer, urothelial carcinoma can start in any part of the urinary system lined with urothelium, including the urethra and the upper urinary tract (renal pelvis and ureters). Upper urinary tract cancer and urethral cancer are managed differently than bladder cancer, and are beyond the scope of this book.

The start and spread of bladder cancer

We learned that the inside lining of the bladder is the urothelium, which is made of urothelial cells (also called transitional cells). If urothelial cells start to make too many copies of themselves and grow uncontrollably, this is bladder cancer.

After forming in the urothelium, tumors grow into the bladder wall, as if to “escape” the bladder. Cancer cells can then travel through blood or lymph to form new tumors in other parts of the body. This is called metastasis.

Three phases of bladder cancer

People with bladder cancer can be grouped into three main categories, depending on how far the cancer has spread. The treatment goals and management of these groups are different.

Non-muscle invasive bladder cancer

Stages 0 and 1 are non–muscle-invasive. This is early bladder cancer. The tumor has not reached the thick layer of muscle in the bladder wall, which has a containment function in this setting. The goals of treatment for non–muscle-invasive cancer are to:

- Reduce the risk of cancer coming back after successful treatment, and
- Stop the cancer from progressing to a more advanced stage.

Muscle-invasive bladder cancer

Stages 2, 3, and early stage 4 are muscle-invasive. The tumor has invaded the muscle layer of the bladder wall. Local control therapy such as surgery or radiation, potentially combined with chemotherapy, may be needed to prevent the spread of cancer cells far from the bladder. The goals of treatment for muscle-invasive cancer are to:

- Stage the cancer to confirm that it is muscle-invasive, but has not spread to other areas (metastasized).
- Determine the best local treatment option (for example, surgery with chemotherapy or chemoradiation therapy).

Metastatic bladder cancer

Cancer has spread to lymph nodes and organs far from the bladder. These cancers are generally not curable. The main goal of care for metastatic bladder cancer is to help you live as normally and as comfortably as possible, for as long as possible.

Diagnosis and treatment planning

The path to diagnosing bladder cancer usually starts with finding blood in the urine (hematuria). See

Figure 3. The presence of blood can cause your urine to change color, which is one way that hematuria is found. If there is only a small amount of blood in the urine, hematuria may only be found during a urinalysis.

Some people may notice that they have to urinate (pee) more often than usual (frequent urination) and/or that the need to urinate comes on quickly and is very intense (urgent urination). Many people also experience pain while urinating. Bladder cancer can also cause pain in the low back and pelvis.

If your doctor suspects that you may have bladder cancer, he or she will want to do testing. The following tests are recommended by NCCN experts to diagnose (or rule out) bladder cancer.

Health history and physical exam

Your doctor will need to know a lot about your past and current health. He or she will ask you about:

- Illnesses, diseases, and surgeries you've had
- Medicines that you take (prescription or over-the-counter)
- Your lifestyle (your diet, how much exercise you get, and whether you smoke or drink alcohol)
- Symptoms that could be related to bladder cancer

Your doctor will also do a physical exam of your body to look for general signs of disease.

Cystoscopy

Cystoscopy is a procedure to see inside the bladder and other organs of the urinary tract using a tool inserted through the urethra. **See Figure 4.**

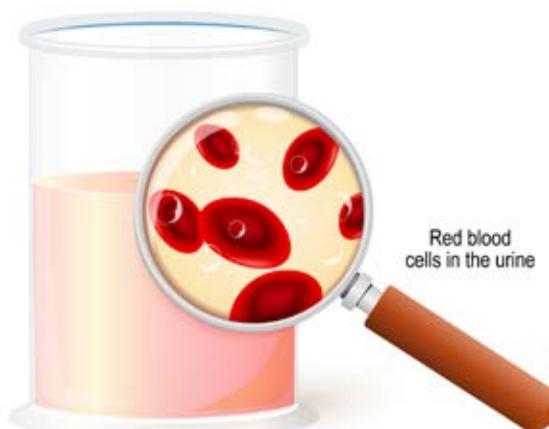
Cystoscopy may be done in your doctor's office at the initial (first) visit, or it may be scheduled for a date in the near future. If your doctor sees any suspicious areas during the cystoscopy, more testing is needed. The other tests you should have are described next.

Urine cytology

Urine cytology is a simple, noninvasive way to look for bladder cancer. It involves examining a sample of your urine under a microscope to look for cancer cells.

Figure 3. Hematuria

The most common symptom of bladder cancer is blood in the urine. This is called hematuria.



Imaging of the abdomen and pelvis

NCCN experts recommend having computed tomography (CT or “cat scan”) or magnetic resonance imaging (MRI) of your abdomen and pelvis. These imaging studies can help determine the extent of the cancer, including whether it has spread beyond the bladder.

Bimanual examination under anesthesia

This procedure allows your doctor to feel and examine your bladder and nearby organs with both hands from inside your body. This helps to stage the cancer and understand the extent of spreading. General anesthesia is used for the procedure, so you will be asleep and not feel any discomfort.

Transurethral resection of the bladder tumor (TURBT)

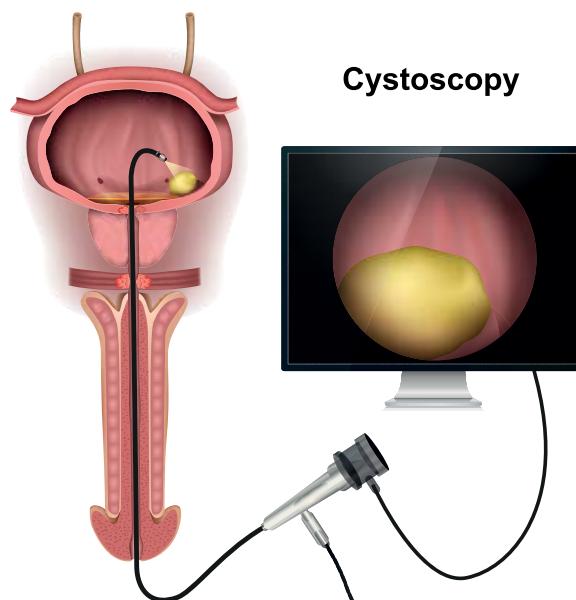
TURBT is a procedure that allows your doctor to remove and examine tumors on the bladder wall through the urethra, without cutting through the abdominal/pelvic skin. An instrument with a small cutting tool at one end is guided through the urethra and into the bladder to remove the tumor. This is done in the operating room under general anesthesia.

Goals of TURBT:

- To make or confirm the diagnosis and histology of bladder cancer
- To determine how extensive the cancer is inside the bladder
- To remove all of the tumor that can be seen

Figure 4.
Cystoscopy being performed on a man

Cystoscopy is used to see inside the bladder and urethra without cutting into the body. Cystoscopy is performed using a hollow tool with a magnifying lens at one end, called a cystoscope.



- To take a sample of the muscle layer of the bladder wall to see if the tumor has invaded muscle

If the cancer is thought to be non-muscle-invasive based on the TURBT, NCCN experts recommend a one-time dose of chemotherapy be put directly into your bladder very soon after the TURBT. This is called intravesical, or local, chemotherapy. Immediate local chemotherapy to the bladder after TURBT can help reduce the chances of non-muscle-invasive bladder cancer returning after treatment.

Chemotherapy should be given within the 24 hours following TURBT (ideally within 6 hours). Gemcitabine and mitomycin C are the most commonly used medicines for intravesical chemotherapy. Gemcitabine is preferred by NCCN experts over mitomycin C.

Biopsies of other areas

If the tumor has high-risk features, your doctor may want to do biopsies of nearby areas or organs, including the prostate in men.

Extra workup for muscle-invasive disease

If initial testing shows that the tumor has invaded the muscle layer of the bladder wall, more testing is recommended. This additional testing should include:

Laboratory testing (bloodwork)

A complete blood count (CBC) is a common blood test that provides information about the numbers and kinds of cells in the blood, including red blood cells, white blood cells, and platelets.

Blood chemistry tests are also recommended and should include alkaline phosphatase (ALP). High levels of ALP may mean that the cancer has spread to bones or the liver.

Bloodwork may also include other tests that assess how well your liver and kidneys are working, as well as how your blood clots (coagulates).

Imaging tests to look for metastases

Your chest should be examined for signs that the cancer has spread if you have muscle-invasive bladder cancer. This can be done using a chest x-ray or CT. If not already done, you should also have imaging of your abdomen and pelvis with either CT or MRI. If CT is being used, it's possible to examine all three areas in one visit.

If you have bone pain or your test results suggest that cancer may have spread to bone, a bone scan is recommended.

Biomarker testing

An additional type of test sometimes recommended by NCCN experts for people whose cancer has spread beyond the bladder and can't be removed with surgery is biomarker (also called tumor marker) testing. Tumor markers can be substances, like molecules or proteins, that are made by your body because you have cancer. Tumor markers can also be processes, such as the way your DNA "acts" that makes it unique. The most important biomarkers in bladder cancer treatment are described next.

PD-L1 expression. Your immune system has important white blood cells called T cells. T cells' main job is to attack harmful things in your body, like bacteria, viruses, and cancer cells. They do this with the help of a protein on their surface called programmed cell death-1 (PD-1) receptor.

Cancer cells have a different protein on their surface called PD-L1 (programmed death-ligand 1). When the PD-1 receptor and PD-L1 meet, it is called an immune checkpoint. The T cell is "told" to leave the cancer cell alone instead of attacking it.

A PD-L1 test measures how much PD-L1 a tumor makes. Knowing this about your tumor helps your doctor decide if treatment with drugs called immune checkpoint inhibitors may help you. Immune checkpoint inhibitors stop these two proteins from meeting. This means that the T cells will do their job and attack the cancer cells.

If your tumor is positive for PD-L1, it doesn't automatically mean that treatment with an immune checkpoint inhibitor is a good treatment option for you. There are other factors that your doctors will consider before recommending (or not recommending) treatment with an immune checkpoint inhibitor.

Fibroblast growth factor receptor (FGFR)

inhibition. Many people with the most common type of bladder cancer (urothelial carcinoma) have altered versions of the *FGFR2* and *FGFR3* genes. If you have alterations of either of these genes and your cancer has progressed on platinum-based chemotherapy (eg, cisplatin or carboplatin), you may be eligible for treatment with a targeted therapy drug called erdafitinib (BALVERSA™).

Next steps

Your doctors will use the results of all the tests just described in order to determine the stage of the cancer. The staging process is described in the next section.



Did you know...

...that **smoking cigarettes** is the BIGGEST risk factor for bladder cancer?

A risk factor is anything that increases the chances of getting a disease.

Smoking also raises the risk of getting other types of cancer and diseases.

It's never too late to quit

Quitting at ANY TIME will greatly benefit your health and can reduce the chances of getting many serious diseases and other cancers.

What you can do

If you have bladder cancer and are still smoking – **QUIT!**

Help is available to people who want to stop smoking. Ask your treatment team about resources and programs that can help you break the habit.

Helpful websites

[Quitting Smoking - Centers for Disease Control and Prevention \(CDC\)](#)

[Fact or Fiction: What to Know about Smoking Cessation and Medications](#)

[Smokefree.gov](#)

Review

- The bladder is part of the urinary system. Urine is stored in the bladder until it leaves the body during urination.
- The most common type of bladder cancer is called urothelial carcinoma because it starts in urothelial cells that line the inside of the bladder. Another name for urothelial carcinoma is transitional cell carcinoma.
- There is a thick layer of muscle in the bladder wall called the detrusor muscle, or the muscularis propria. If the tumor reaches and invades this layer, it is called muscle-invasive bladder cancer.
- Cancer can spread through lymph and blood to form tumors in other parts of the body. This is called metastasis.
- Initial testing for suspected bladder cancer includes cystoscopy, cytology, imaging of the abdomen and pelvis, TURBT, and examination of the bladder under anesthesia.
- If muscle-invasive disease is suspected, more testing is needed. This includes bloodwork and imaging tests to look for metastases in the chest, and maybe also the bones.
- Biomarker testing is recommended for people with bladder cancer that has spread beyond the bladder and cannot be removed with surgery. Having specific genetic alterations may mean you are a candidate for certain targeted therapies or immunotherapies.
- Smoking is the biggest risk factor for bladder cancer! If you have bladder cancer and are still smoking—it's not too late to quit. Ask your treatment team for help.

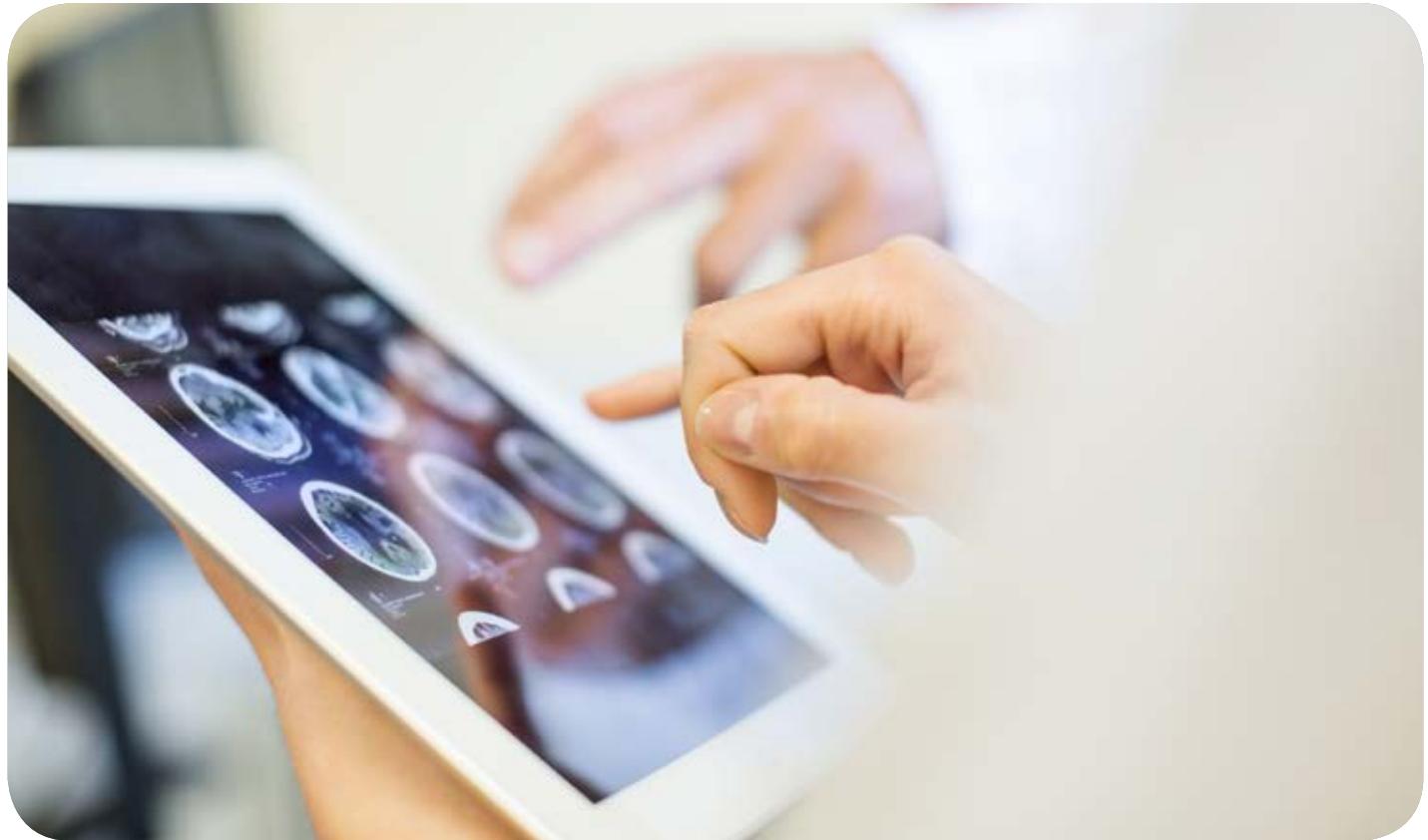
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Staging bladder cancer

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You have likely heard the word “stage” when talking about cancer. The stage is a rating of how far the cancer has grown so far. The cancer stage is used to decide which tests and treatments will help you most.

How bladder cancer is staged

Bladder and other cancers are often staged twice, both initially and with information gained during surgery to remove the bladder.

Clinical (pre-surgery) stage

The clinical stage is a rating of how much cancer is in the body based on a physical exam, blood tests, and initial biopsies. In the case of bladder cancer, the clinical stage is based on the examination under anesthesia (EUA), TURBT, and imaging studies.

Pathologic (post-surgery) stage

The pathologic stage is a rating of the extent of cancer based on more definitive information gained during surgery to remove the bladder and nearby lymph nodes and organs (radical cystectomy).

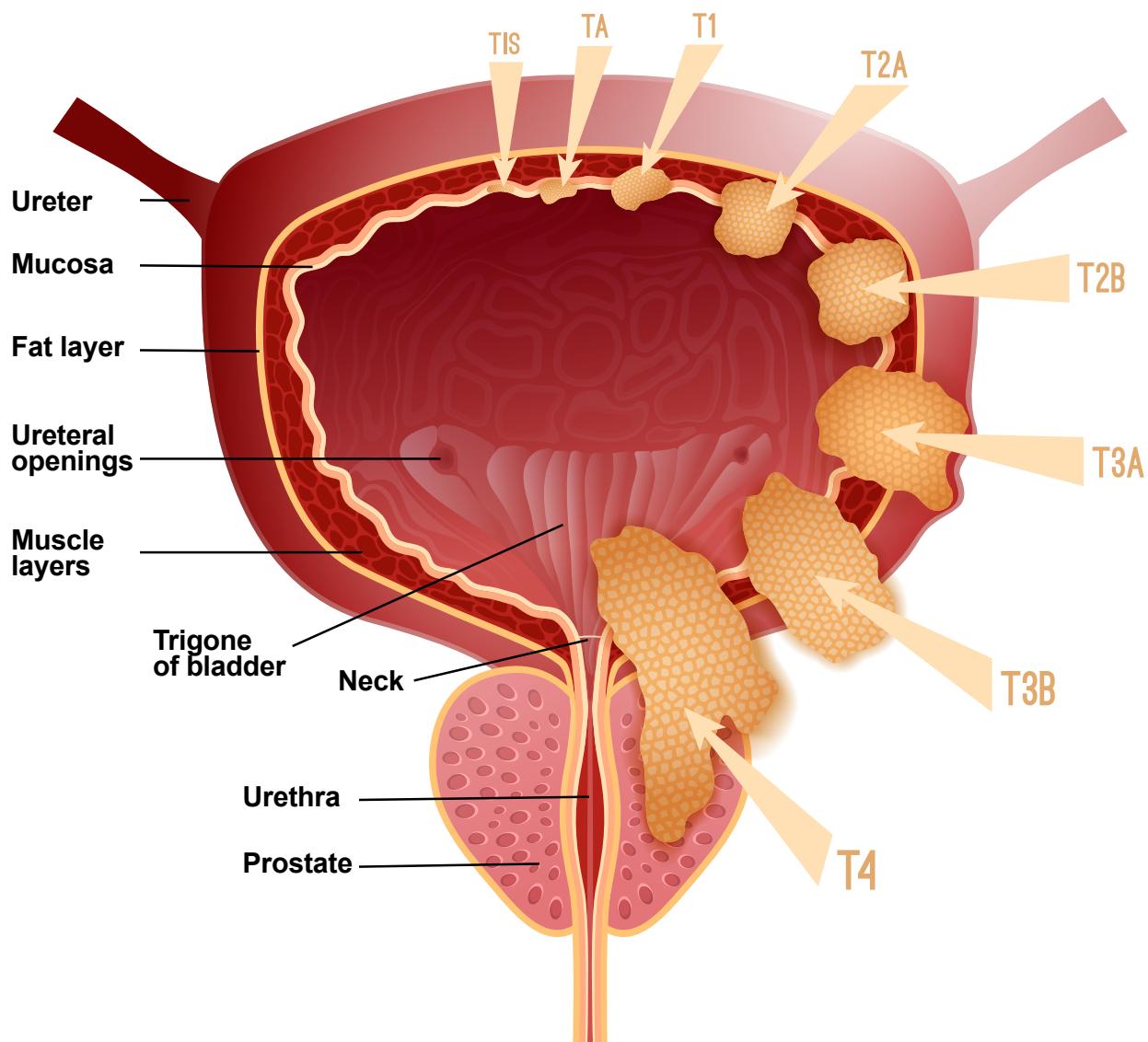
The most commonly used staging system for bladder cancer is the tumor, node, metastasis (TNM) system developed by the American Joint Committee on Cancer (AJCC). This system uses the following key pieces of information about the cancer in order to give it an overall stage.

- **T:** How far the tumor has grown through the bladder wall
- **N:** Whether cancer has spread to nearby lymph nodes
- **M:** Whether the cancer has spread to organs far from the bladder (**metastasized**)

T = Tumor

To describe how far a tumor has grown into the bladder wall, a number from 1 to 4 (and sometimes a letter) is used. The higher the number, the deeper the tumor has grown into the bladder wall. This is called the tumor stage. The tumor stage is not the same as the overall stage, but it plays a major role in determining the overall stage. The tumor stages for bladder cancer are described next and shown in **Figure 5**.

- **T_a tumors** are called “papillary” tumors. Papillary tumors grow towards the inside of the bladder (called the lumen), where urine is held, rather than into the bladder wall. These tumors look like thin, finger-like growths. They are similar in appearance to broccoli stalks.
- **T_{is}** refers to a flat area of fast-growing abnormal cells on the inside lining of the bladder. T_{is} is also called carcinoma in situ. These flat tumors are high-grade and need to be treated because they could become invasive bladder cancer.
- **T₁ tumors** have grown into the connective tissue layer of the bladder wall, but not into the muscle layer. This is non-muscle-invasive bladder cancer.
- **T₂ tumors** have entered the muscle layer of the bladder wall. It may be only in the inner half of the muscle layer (a T_{2a} tumor) or it may have invaded the outer half (a T_{2b} tumor). This and later stages are muscle-invasive bladder cancer.
- **T₃ tumors** have grown all the way through the bladder wall and into the fatty tissue that surrounds the bladder.
- **T₄ tumors** have invaded any of these nearby areas: the prostate, the glands that help produce semen (called the seminal vesicles), the uterus, the vagina, or the wall of the pelvis or abdomen.

Figure 5.**Bladder cancer tumor stages.**

N = Node

There are hundreds of lymph nodes in your body. They work as filters to help fight infection and to remove harmful things from the body. Doctors use a number from 0 to 3 to describe whether bladder cancer has spread to any lymph nodes in the pelvic region. The higher the number, the greater the extent of the lymph node involvement. If your doctors don't know if any lymph nodes have cancer, an X is used instead of a number. See below for the N numbers and what they mean.

- **N0** means that cancer hasn't spread to any nearby lymph nodes.
- **N1** means that cancer has spread to only one lymph node in the pelvis.
- **N2** means that cancer has spread to more than one lymph node in the pelvis.
- **N3** means that cancer has spread to lymph nodes in the upper pelvic region, called the common iliac lymph nodes.

M = Metastasis

Cancer can spread far from the bladder. This process is called metastasis. Knowing whether the cancer has spread far from the bladder is an important part of choosing the best treatments. To describe whether the cancer has spread far (metastasized), either a 0 or a 1 is used. If your doctors don't know if the cancer has spread far, an X is used.

- **MX** means that it is unknown if cancer has spread far from the bladder.
- **M0** means that the cancer hasn't spread from your bladder.
- **M1** means that the cancer has spread to either distant lymph nodes (M1a) or to distant organs (M1b).

G = Grade

The next piece of information used to plan treatment for bladder cancer is called its grade. The grade is a rating of how fast your doctors think the cancer will 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 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).

Putting it all together

We just learned about these four key pieces of information your doctors need to know about your cancer:

- How far the tumor has grown through the bladder wall (the tumor stage)
- Whether any nearby lymph nodes are suspected of having cancer
- Whether the cancer has spread to lymph nodes or organs far from the bladder
- How fast the cancer is expected to grow (the tumor grade)

These four things are then combined to give the cancer a stage. It is important to know that two people with bladder cancer may be the same stage, even though their cancers are not exactly the same. In other words, there can be more than one definition of a stage. Knowing the stage is critical to selecting the right treatment.

Stages of bladder cancer

There are 5 main stages of bladder cancer: 0, 1, 2, 3, and 4. Some of these stages are broken down into sub-groups. **See Figure 6.** The staging information provided next is based on the 8th edition of the AJCC *Cancer Staging Manual*.

Non-muscle invasive stages

Stage 0a

One or more papillary tumors have formed on the inside lining of the bladder. Cancer hasn't spread to lymph nodes or organs far from the bladder. This is the earliest stage of bladder cancer.

Stage 0is

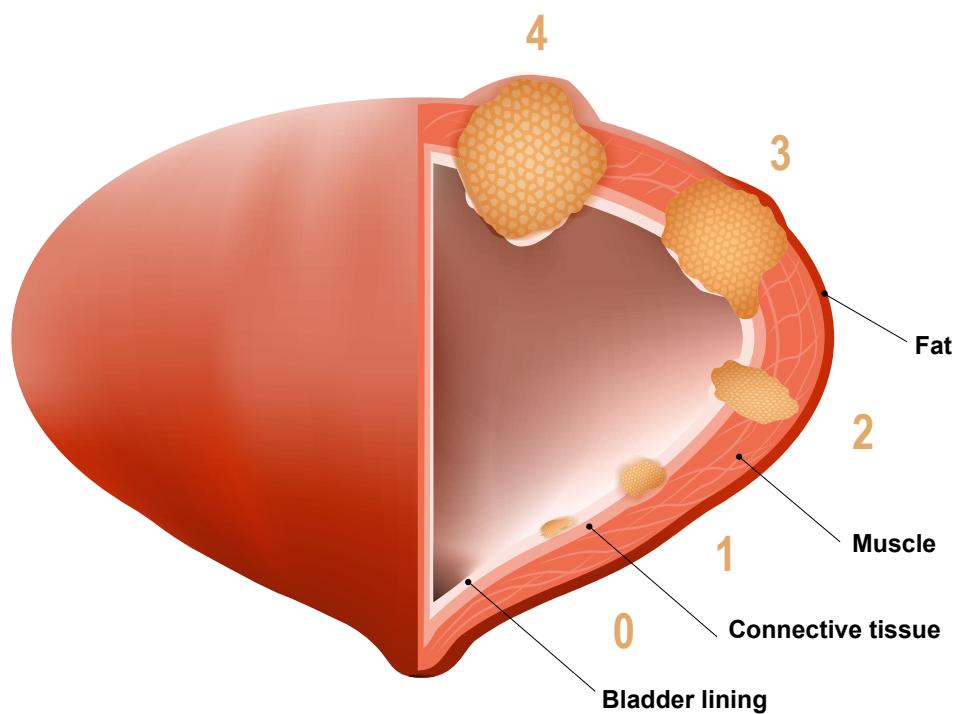
There are flat areas of fast-growing abnormal cells called carcinoma in situ (CIS) on the inside lining of the bladder. Cancer hasn't spread to lymph nodes or organs far from the bladder.

Stage 1

The tumor has grown into the second layer of the bladder wall (made of connective tissue) but has not reached the muscle layer. Cancer hasn't spread to lymph nodes or organs far from the bladder.

Figure 6.

The stages of bladder cancer.



Muscle-invasive stages

Stage 2

The tumor has invaded the muscle layer of the bladder wall. It may be only in the inner half of the muscle layer (a T2a tumor) or it may have invaded the outer half (a T2b tumor). Cancer hasn't spread to lymph nodes or organs far from the bladder.

Stage 3A

There are two main scenarios for this cancer stage:

Scenario 1. The tumor has grown through the bladder wall. It may be only in the fatty tissue surrounding the bladder, or it may have invaded nearby organs or structures. Cancer hasn't spread to lymph nodes or organs far from the bladder.

Scenario 2. The tumor may be small or large. Cancer has spread to one nearby lymph node in the pelvis. Cancer hasn't spread to lymph nodes or organs far from the bladder.

Stage 3B

The tumor may be small or large. Cancer has spread to multiple lymph nodes in the pelvis, or to lymph nodes in the upper pelvic region. Cancer hasn't spread to lymph nodes or organs far from the bladder.

Stage 4A

There are two main scenarios for this cancer stage:

Scenario 1. The tumor has grown through the bladder wall and has invaded the wall of the pelvis or abdomen. The primary tumor cannot be removed with surgery. There may be cancer in nearby lymph nodes, but not in distant lymph nodes or organs.

Scenario 2. The tumor may be small or large. Cancer has spread to lymph nodes (but not organs) far from the bladder.

Stage 4B

The tumor may be small or large. Cancer has spread to lymph nodes and organs far from the bladder, like the bones, liver, or lungs. This is distant metastatic bladder cancer.

Review

- The most commonly used staging system for bladder cancer is the TNM system. There are 5 overall stages of bladder cancer: 0, 1, 2, 3, and 4.
- Stage 0 is the presence of abnormal cells on the inside lining of the bladder. Stage 1 disease means that a tumor has formed and has invaded the layer of connective tissue in the bladder wall. These are non-muscle-invasive cancers.
- Stage 2 and higher 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 surrounding the bladder. There may be cancer in nearby lymph nodes.
- In stage 4 disease the cancer has spread to lymph nodes or organs far from the bladder. Or it hasn't spread to distant areas but has invaded the wall of the abdomen or pelvis and can't be removed with surgery.

3

Treatments for bladder cancer

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This chapter describes the main treatments for bladder cancer. The best treatment(s) for you will depend on the cancer stage and your preferences. Using more than one type of treatment (combination therapy) is common.

Surgery

TURBT

TURBT is a procedure that allows your doctor to remove and examine tumors on the bladder wall through the urethra, without having to cut through the abdominal/pelvic skin. An instrument with a small cutting surface at one end is guided through the urethra and into the bladder to remove the tumor. This is done under general anesthesia in an operating room.

Goals of TURBT:

- To make or confirm the diagnosis and histology of bladder cancer
- To determine how extensive the cancer is inside the bladder
- To remove all of the visible tumor
- To take a sample of the muscle layer of the bladder wall to see if the tumor has invaded muscle

Radical cystectomy

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. The other organs that are removed are different for men and women.

In men, the following organs are also removed:

- The prostate
- The glands that help make semen (called the seminal vesicles)
- Part of the vas deferens. The vas deferens is a tube that carries sperm away from the testicles.
- The part of the urethra that goes through the prostate (called the proximal urethra)

In women, the following organs are also removed:

- The uterus
- The ovaries
- The fallopian tubes
- The urethra
- Part of the vagina

Because the bladder is removed during a radical cystectomy, both men and women will need a new way to store urine and for urine to leave the body. This is done using a surgical procedure called a urinary diversion. This can be done in different ways. The three main types of urinary diversions are described next. Your surgeon and treatment team can explain the options for redirecting urine and help you choose the option that's right for you.

Ileal conduit

The last portion of the small intestine is called the ileum (pronounced ill-ee-um). One way to reroute urine after a radical cystectomy is to remove part of the ileum and use it as a pipeline (conduit). To do this, one end of the ileum is attached to the ureters, much like your bladder was. The other end is attached to a small hole made in the wall of your abdomen, called a stoma. Urine flows through the hollow, tube-like ileum and out of the body through the stoma.

A small disposable bag attached to the outside of your abdomen collects urine when it comes out of the stoma. This is called an ostomy bag (or ostomy pouch). The bag stays attached to your body with the help of an adhesive part called a “wafer.” The wafer sticks to the skin and acts as a watertight barrier.

When you had your bladder, you peed when your bladder was full, likely between 6 to 8 times a day. With an ileal conduit, urine constantly trickles out of the stoma. This means that you must wear an ostomy bag at all times. Most people find that they need to empty the bag every 2 to 4 hours, depending on how much liquid they drink. An opening or valve at the bottom of the bag allows the urine to be emptied into a toilet without taking off the bag. Larger capacity ostomy bags are available for overnight use.

Neobladder

This type of urinary diversion also involves removing part of your small intestine. Instead of serving as a tunnel for urine to travel through (like an ileal conduit), the piece of intestine is made into a hollow pouch to hold urine. Like your original bladder, this substitute bladder is attached to the ureters at one end and your 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. This approach does not use a stoma or require an ostomy bag, since urine leaves the body in the usual way.

Neobladders don't work in the same way as real bladders. They can make it hard to control the flow of urine out of the body. In other words, urine might come out when you don't want it or expect it to, particularly during sleep. This is called urinary incontinence.

Substitute bladders can also have trouble emptying completely. Some people may need to have a catheter inserted through their urethra to help drain the urine from a substitute bladder.

Continent urinary reservoir (Indiana pouch)

This type of urinary diversion is often referred to as an “Indiana pouch” because it was developed by doctors at Indiana University. Creating an Indiana pouch entails using a piece of your intestine to create a small pocket, or reservoir, in the wall of your abdomen and a valve to keep urine in the pouch. Urine flows directly from the ureters into this reservoir. A tiny hole called a stoma is made in the abdominal wall at the location of the reservoir. A catheter must be inserted through the stoma and into the reservoir several times a day to drain the urine. Sometimes the stoma (hole) can be made in the belly button, making it much less noticeable.

A benefit to this type of urinary diversion, as with a substitute bladder, is that an ostomy bag doesn't need to be worn on the outside of the body. This may be appealing to people with concerns about body image, and those who don't want to worry about an ostomy bag coming loose or leaking.



I was horrified and scared when diagnosed. I would have done ANYTHING to save my bladder. But I needed a cystectomy and now have an Indiana pouch. I lead a normal life, swimming and even scuba diving. The thing to remember is that your LIFE IS MORE IMPORTANT THAN YOUR BLADDER.

— Cynthia, age 62

14-year bladder cancer survivor

Partial cystectomy

A partial cystectomy is a surgical procedure to remove part of the bladder. It is not widely used for the treatment of bladder cancer. Fewer than 5 out of 100 people will meet the criteria for a partial (instead of a radical) cystectomy.

You may be eligible for a partial cystectomy if:

- The tumor is at the top of the bladder and there are no fast-growing (high-grade) cells in other areas of the bladder lining.
- The cancer is only in a small pouch sticking out from the bladder wall (called a diverticulum).
- You have other very serious health conditions that would prevent you from having a radical cystectomy.

Intravesical therapy

Intravesical therapy is the use of medicines put directly into the bladder through a catheter. The medicines are slowly put into the bladder using a process called instillation. There are two main intravesical therapies used to treat bladder cancer:

- Intravesical Bacillus Calmette-Guérin (BCG) therapy
- Intravesical chemotherapy

Intravesical BCG therapy

BCG therapy uses a liquid solution put directly into your bladder. The solution contains a very weak version of a bacterium (germ) that has been used as a tuberculosis vaccine in many parts of the world. Researchers aren't sure why, but the solution can jumpstart your immune system and cause it to attack cancer cells inside the bladder without giving you tuberculosis.

Intravesical BCG may cause flu-like symptoms for 48 to 72 hours after instillation. It may also cause symptoms similar to a urinary tract infection, including pain while urinating. Some people cannot tolerate the side effects of intravesical BCG. However, the side effects are usually treatable. There are medications available that have been shown to lessen the side effects of BCG. It is also possible to adjust the amount of BCG given in order to help with side effects.

As a primary (main) treatment

Another name for treatment given first and that is expected to work the best is "induction therapy." When used as the main treatment for non-muscle-invasive disease after TURBT, intravesical BCG can help lower the chance of the cancer coming back and lower the risk of the cancer becoming muscle-invasive. Intravesical BCG has been shown to be better at preventing the return of cancer than TURBT alone or TURBT with chemotherapy. BCG is usually started 3 to 4 weeks after TURBT. It is given once a week for 6 weeks, followed by a rest period of 4 to 6 weeks. You should have a full re-evaluation 12 weeks after the date you start treatment.

As a maintenance treatment

If primary treatment with intravesical BCG succeeded at killing all the cancer cells, research has shown that continuing BCG for an extended period may reduce the risk of cancer returning. If you had BCG as the primary treatment after TURBT and no cancer was found at the follow-up cystoscopy, NCCN experts recommend continuing BCG therapy in most cases. This is called maintenance BCG therapy.

Most patients receive maintenance intravesical BCG for 1 to 3 years, depending on the individual risk of the cancer returning. One year of maintenance BCG is likely appropriate for those at intermediate (average) risk of the cancer returning. Those at high risk of recurrence should have 3 years of maintenance therapy.

Intravesical (local) chemotherapy

Intravesical chemotherapy is given to reduce the risk of the cancer coming back, or to slow cancer's growth to a higher stage. Gemcitabine and mitomycin C are the most commonly used intravesical chemotherapies. Gemcitabine is preferred by NCCN experts over mitomycin C. Other chemotherapy agents may be used by your doctor in certain circumstances.

Immediately after TURBT

When given immediately after TURBT, a one-time dose of intravesical chemotherapy can lower the risk of cancer returning. The one-time instillation should be given within 24 hours of surgery (ideally within 6 hours).

As a primary (main) treatment

While intravesical BCG therapy is used more often as a primary (main) treatment option after TURBT for non-muscle-invasive bladder cancer, intravesical chemotherapy is also an option. Treatment is usually started 3–4 weeks after TURBT. The treatments are usually given weekly for about 6 weeks. NCCN experts recommend no more than two back-to-back courses of treatment.



BCG shortage!

Did you know that only one supplier is currently approved to provide BCG in the United States?

Unfortunately, this means that it can't always make enough to treat everyone with non-muscle-invasive bladder cancer who needs it.

When there isn't enough BCG to go around, priority goes to people with high-risk NMIBC.

For everyone else, there are other options your doctors may suggest. They include:

- ✓ Treatment with intravesical chemotherapy instead
- ✓ Using a reduced dose of BCG
- ✓ Going straight to surgery (for those at high risk of the cancer returning after treatment)
- ✓ Joining a clinical trial

Systemic therapy

A cancer treatment that affects the whole body is called systemic. The most common type of systemic therapy is chemotherapy. Chemotherapy and other types of systemic therapy are described next.

Chemotherapy

Chemotherapy is treatment with drugs to kill cancer cells. Most chemotherapy drugs are liquids that are slowly injected into a vein. This process is called infusion. The drugs travel in your bloodstream to treat cancer throughout your body. Chemotherapy also harms healthy cells, which is why it can cause very harsh side effects.

Some chemotherapy medicines contain the metal platinum. Platinum-based chemotherapy medicines can damage the kidneys. Cisplatin and carboplatin are two platinum-based chemotherapy medicines used to treat bladder cancer. Cisplatin is the stronger of the two medications and more likely to harm the kidneys than carboplatin. Many people can't have cisplatin because their kidneys don't work well or because of other health issues. Cisplatin may also cause hearing problems or loss.

In order to determine which systemic therapy medicines are 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.

Targeted therapy

Targeted therapy is a cancer treatment that can target and attack specific types of cancer cells. This type of cancer treatment is often used for people with specific gene mutations. If you don't have the mutation that the medicine "targets," treatment is unlikely to help you. For example, erdafitinib (BALVERSA™) is a targeted therapy used for

Did you know?

The terms "chemotherapy" and "systemic therapy" are often used interchangeably. This is because chemotherapy is the most common type of systemic therapy. However, newer treatments, like targeted therapy and immunotherapy, also affect the whole body but work differently than chemotherapy.

bladder cancer that targets mutations of specific genes called the *FGFR2* and *FGFR3* genes.

Because targeted therapy does not harm normal cells as much as chemotherapy, the side effects tend to be less severe.

Immunotherapy

Immunotherapy is a cancer treatment that increases the activity of your body's immune system. By doing so, it can improve your body's ability to find and destroy cancer cells. Immunotherapy medicines called checkpoint inhibitors are used to treat bladder and other cancers.

Radiation therapy

Radiation therapy uses high-energy waves similar to x-rays to kill cancer cells. 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. **See Figure 7.**

Systemic therapy and radiation therapy are often used together to treat bladder cancer. This is called chemoradiation or chemoradiotherapy.

Clinical trials

New tests and treatments aren't offered to the public until they are deemed safe for testing and potentially effective. They first need to be studied in a way that is regulated by the FDA and other governmental

agencies. A clinical trial is a type of research that studies how safe and effective tests and treatments are and they are done at all stages of a disease like bladder cancer. When found to be safe and effective, they may become tomorrow's standard of care. Because of clinical trials, the tests and treatments in this book are now widely used to help people with bladder cancer. All new drugs are tested in a clinical trial before being approved for general use.

Joining a clinical trial can have both upsides and downsides. You will need to weigh the potential benefits and downsides to decide what is right for you. To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial are often alike in terms of their cancer and general health. This is to ensure that any progress is because of the treatment and not because of differences between patients.

Figure 7.

External beam radiation therapy.



To join, you'll need to review and sign a paper called an informed consent form. This form describes the study in detail. The study's risks and benefits should be fully described.

Ask your treatment team if there is an appropriate clinical trial that you can join. There may be clinical trials where you're getting treatment or at other treatment centers nearby. You can also find clinical trials through the websites listed in Part 7, *Making treatment decisions*.

Review

- Radical cystectomy is the most effective and widely used surgery for muscle-invasive bladder cancer. It involves removing the bladder, nearby lymph nodes, and other nearby organs.
- A partial cystectomy is a surgical procedure to remove part of the bladder. It is used in specific patients for the treatment of bladder cancer.
- Intravesical therapy is the use of medicines put directly into the bladder. The two main intravesical therapies used to treat bladder cancer are BCG therapy and intravesical chemotherapy.
- A cancer treatment that affects the whole body is called systemic. Chemotherapy, targeted therapy, and immunotherapy are types of systemic therapies.
- Radiation therapy uses high-energy waves similar to x-rays to kill cancer cells. Radiation therapy is often used together with chemotherapy. This is called chemoradiation or chemoradiotherapy.
- A clinical trial is a type of research that studies how safe and effective tests and treatments are. When found to be safe and effective, they may become tomorrow's standard of care.

Did you know?

✓ NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

4

Non–muscle-invasive bladder cancer

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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. Treatment of these cancers is focused on reducing the chance of cancer coming back after successful treatment and preventing progression to a more advanced stage.

Stage 0

Stage 0 bladder cancer includes two types of tumors: Ta (papillary) and carcinoma in situ (CIS).

Ta (papillary) tumors

Treatment of papillary tumors depends on whether they are fast- or slow-growing (high- or low-grade).

Slow-growing Ta tumors

After TURBT and the one-time chemotherapy dose to your bladder, some slow-growing (low-grade) papillary tumors may need more treatment. The decision to have more treatment should be based on the risk of the cancer returning. Below are some factors that your doctor will consider in order to determine if you should have more treatment.

- How many tumors there are, and how big they are
- How deep the tumor(s) has grown into the bladder wall
- If the tumor returned after treatment
- If there is also carcinoma in situ (CIS)

If more treatment is needed, six weeks of intravesical (local) chemotherapy is recommended. The most common medicines used for intravesical

chemotherapy are gemcitabine and mitomycin C. Gemcitabine is preferred by NCCN experts over mitomycin C.

Fast-growing Ta tumors

After TURBT and the one-time chemotherapy dose to the bladder, most fast-growing (high-grade) papillary tumors will need more treatment. This may include another TURBT as the first step. There are two main reasons why a second TURBT may be necessary:

- The first TURBT didn't remove all of the cancer. In this case, NCCN experts recommend a second TURBT.
- There wasn't any muscle in the tissue removed for testing during the first TURBT. In this case, NCCN experts strongly encourage a second TURBT.

Options for treatment after the first (and possibly second) TURBT are:

- Intravesical BCG therapy (**preferred by NCCN experts**)
- Intravesical (local) chemotherapy
- Watch-and-wait (no treatment)

Among the three treatment options above, BCG therapy is preferred by NCCN experts. If BCG therapy is used, it is a good idea to continue maintenance BCG therapy.

Carcinoma in situ

Any areas of CIS need to be treated because they could become invasive bladder cancer. After TURBT, NCCN experts recommend treating these flat areas of fast-growing cells with intravesical BCG therapy.

The treatment options described above for stage 0 bladder cancer are summarized in [Guide 1](#).

Guide 1. Stage 0: Treatment options after TURBT

Tumor type		Next treatment options
Slow-growing Ta tumor		<ul style="list-style-type: none">• Observation• Intravesical chemotherapy
Fast-growing Ta tumor		<p>Before beginning further treatment, you may need a second TURBT.</p> <p>Next treatment options:</p> <ul style="list-style-type: none">• Intravesical BCG therapy (preferred)• Intravesical chemotherapy• Observation
Carcinoma in situ (CIS)		Intravesical BCG therapy

“ ”

BCG treatments are very “do-able” and life-saving in the case of high-grade noninvasive bladder cancer. There is nothing to be afraid of!

– Nancy Anne, age 81
11-year bladder cancer survivor

Stage 1

In stage 1 bladder cancer the tumor has grown into the second layer of the bladder wall. Many of these tumors are fast-growing (high-grade) and likely to come back after treatment. Because of the high-risk nature of these tumors, the first TURBT you had may not have removed all of the cancer. For this reason, NCCN experts strongly recommend that most people with stage I bladder cancer have another TURBT.

The second TURBT found cancer

If you have a second TURBT, further treatment will depend on whether cancer cells are found and how deep they are in the bladder wall. If cancer is found during the second TURBT, there are two treatment options:

- Intravesical BCG therapy
- Surgery (radical cystectomy)

Most people can be safely and effectively treated with intravesical BCG therapy. If BCG therapy is used, it is a good idea to have maintenance BCG therapy. Maintenance BCG therapy may continue for years. People at higher risk, however, will need surgery to remove the bladder (radical cystectomy). For example, surgery may be needed if the second TURBT found that a high-grade tumor has grown into the muscle layer of the bladder wall. For people who are not candidates for surgery, having chemoradiation (chemo and radiation together) is an option. [Guide 7](#) on page 43 lists the recommended chemotherapy regimens to be used with radiation if you're not having surgery.

The second TURBT didn't find cancer

If cancer is not found during the second TURBT, most people will have two treatment options:

- Intravesical BCG therapy (preferred by NCCN experts)

➤ Intravesical (local) chemotherapy

BCG therapy is preferred over local chemotherapy by NCCN experts. If BCG therapy is used, it is a good idea to have maintenance BCG therapy.

If local chemotherapy is used, the most common medicines used are gemcitabine and mitomycin. Gemcitabine is preferred by NCCN experts over mitomycin.

In very rare cases, more treatment may not be needed if no cancer cells were found during the second TURBT. This may be the case if the tumor is small and didn't grow very far into the second (connective tissue) layer of the bladder wall. There should also be no areas of carcinoma in situ (CIS).

Straight to surgery (no second TURBT)

Most people with stage I bladder cancer will be treated with another TURBT. Some people with very fast-growing tumors, however, may need to have surgery to remove the bladder (radical cystectomy) instead of another TURBT. Some reasons why removing the bladder may be needed include:

- There is more than one tumor in the same area or multiple areas of the bladder
- The tumor is a rare subtype of bladder cancer that usually leads to poor outcomes
- There are tumor cells in the blood or lymph vessels outside of the main tumor (called lymphovascular invasion)

The treatment options described above for stage 1 bladder cancer are summarized in [Guide 2](#).

**SNAPSHOT**

Non-muscle-invasive bladder cancer (NMIBC)

- ✓ Includes stage 0 and stage 1 bladder cancer
- ✓ These tumors have not invaded the muscle layer of the bladder wall
- ✓ After TURBT, NMIBC is usually treated with medicines put directly into the bladder (intravesical therapy)
- ✓ People at high risk may need surgery to remove the bladder and nearby organs (radical cystectomy)

Guide 2. Stage 1: Treatment options after TURBT

Treatment options	Next steps
Option 1 Another TURBT Best option for most people	If the cancer is still there , next treatment options include: <ul style="list-style-type: none">• Intravesical BCG therapy• Surgery (radical cystectomy) If you aren't a candidate for surgery , options include: <ul style="list-style-type: none">• Chemoradiation• Joining a clinical trial
Option 2 Surgery (radical cystectomy) Best option for very-high-risk tumors	If the cancer is gone , next treatment options include: <ul style="list-style-type: none">• Intravesical BCG therapy (preferred)• Intravesical chemotherapy• No treatment (in rare cases)

Follow-up care

When you have finished treatment, the next phase of cancer care will begin. This is the surveillance phase. During this time, it is important to have testing to monitor for the return of cancer. The specific tests you should have—and how often you should have them—are guided by the risk of the cancer returning.

NCCN experts use a system developed by the American Urological Association (AUA) to determine whether there is a low, intermediate (average), or high risk that cancer will return. [See Guide 3](#) for definitions of the three risk levels. Ask your treatment team to help you determine whether you are at low,

intermediate, or high risk of the cancer coming back. [See Guide 4](#) for the recommended follow-up tests according to risk level.

Guide 3. Risk level definitions for non-muscle-invasive disease

Risk level	Description
Low risk	<ul style="list-style-type: none"> You have one slow-growing Ta tumor that is 3 cm (about the size of a strawberry) or smaller You have a tumor that is unlikely to turn into bladder cancer, called a papillary urothelial neoplasm of low malignant potential (PUNLMP)
Medium risk	<ul style="list-style-type: none"> You have a slow-growing Ta tumor that came back during the first year after treatment You have one slow-growing Ta tumor larger than 3 cm (about the size of a strawberry) You have a slow-growing multifocal Ta tumor You have a fast-growing Ta tumor that is 3 cm (about the size of a strawberry) or smaller You have a slow-growing T1 tumor
High risk	<ul style="list-style-type: none"> You have a fast-growing T1 tumor You have a high-grade Ta tumor that came back after treatment You have a high-grade Ta tumor bigger than 3 cm (about the size of a strawberry) or a multifocal Ta tumor There is carcinoma in situ You have a high-grade tumor and BCG therapy didn't work for you You have a rare tumor type There are tumor cells in the blood or lymph vessels outside of the main tumor There are high-grade cancer cells in the part of the urethra that passes through the prostate (only applies to men)

If cancer comes back or spreads

Follow-up cystoscopy found cancer

One of the follow-up tests you will have after bladder cancer treatment is cystoscopy. How often you have cystoscopy and for how many years depends on the risk of the cancer returning. If signs of cancer are found during a cystoscopy, NCCN experts recommend that you have another TURBT. Like the

first TURBT, you should also have a single dose of local (intravesical) chemotherapy within 24 hours of the procedure. The most common medicines used are gemcitabine and mitomycin C. Gemcitabine is preferred by NCCN experts over mitomycin C.

The treatment you receive next depends on how far the tumor has grown through the bladder wall

Guide 4. Follow-up care for non–muscle-invasive disease by risk level

Test	Low risk	Medium risk	High risk
Cystoscopy	Year 1: At 3 months 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		First year: Baseline imaging with CTU, MRU, IVP, retrograde pyelography, or ureteroscopy After that: As directed by your doctor	Year 1: Baseline imaging, then repeat 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	—	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	—		Your doctor may consider doing this testing in the first two years after treatment.

and whether the tumor is slow- or fast-growing. The treatment options include:

- **Intravesical (local) chemotherapy.** In order to decide if this is the best treatment option for you, your doctor will consider the risk of the cancer returning and the risk of it progressing to muscle-invasive disease.
- **Surgery (radical cystectomy)**
- **Chemoradiation.** This is an option if you are not a candidate for surgery and the tumor is small (Ta or T1). [See Guide 7](#) on page 43 for the recommended chemotherapy regimens to use with radiation. In this situation, chemoradiation has been shown to work better for T1 tumors than for Ta tumors.
- Joining a clinical trial is another option for people who cannot have surgery.

After treatment, you should have a follow-up visit in 3 months. After that, the follow-up visits will be spaced farther apart.

Suspicious follow-up urine cytology

If follow-up urine cytology suggests that cancer may have returned, but imaging tests and cystoscopy are normal, more testing is needed. Some of the tests will look for cancer in other areas, including the prostate and the upper urinary tract. Testing includes biopsies of the bladder, prostate, and upper urinary tract. Cytology of the upper urinary tract is also recommended. Your doctor may elect to perform a procedure called an *ureteroscopy*. This test allows your doctor to examine the lining of your kidneys and ureters.

If the biopsy of the bladder finds cancer, BCG therapy is recommended. If BCG therapy works and the cancer is gone, NCCN experts recommend maintenance BCG therapy. If BCG therapy doesn't work, treatment options include:

- Surgery (radical cystectomy)
- Trying a different intravesical medicine instead of BCG. It is unclear how well other intravesical therapies work in this situation. If more intravesical therapy is used but isn't effective, surgery (radical cystectomy) is recommended.
- Chemoradiation. This is an option if you are not a candidate for surgery. See [Guide 7](#) on page 43 for the recommended chemotherapy regimens to use with radiation.
- Joining a clinical trial

If the biopsy of the prostate finds cancer, treatment of the prostate is needed. If the urine cytology test or the ureteroscopy (if used) finds cancer, then treatment of the upper urinary tract is needed.

If all of the tests are negative, you should have a follow-up visit in 3 months. After that, the follow-up visits will be spaced farther apart. If you had BCG therapy, maintenance BCG therapy is an option.

Cancer returned after intravesical therapy

If a follow-up cystoscopy found cancer and you've already had two rounds of intravesical therapy, you should not have any more right away. Two is the maximum number of back-to-back courses recommended by NCCN experts. Instead, you should have a TURBT to help determine the extent of the cancer.

Like the first TURBT, you should also have a single dose of intravesical (local) chemotherapy within 24 hours of the procedure. The most common medicines used are gemcitabine and mitomycin C. Gemcitabine is preferred by NCCN experts over mitomycin C.

If no leftover cancer cells are found, people who were on BCG therapy should continue to have maintenance BCG. Otherwise, no further treatment is needed.

If the TURBT finds cancer, the treatment you receive next depends on how far the tumor has grown through the bladder wall and whether the tumor is slow- or fast-growing. Treatment options include:

- Switching to a different intravesical therapy
- Surgery (radical cystectomy). This treatment option is preferred by NCCN experts for fast-growing (high-grade) T1 tumors.
- Chemoradiation. This is an option if you are not a candidate for surgery. [See Guide 7](#) on page 43 for the recommended chemotherapy regimens to use with radiation.
- Joining a clinical trial

Review

- Stage 0 and stage 1 bladder cancers are non–muscle-invasive. Many non–muscle-invasive cancers can be treated without removing the bladder.
- Treatment of stage 0 disease after TURBT depends on the tumor type and whether it is fast- or slow-growing. Intravesical therapy (either BCG or intravesical chemotherapy) is an option for all stage 0 tumors.
- NCCN experts strongly recommend that most people with stage I bladder cancer have another TURBT before starting treatment. If the second TURBT finds cancer, BCG therapy and surgery are options. If the second TURBT does not find cancer, BCG therapy and intravesical chemotherapy are options.
- Follow-up care for non–muscle-invasive disease includes testing based on the risk of the cancer returning. The higher the risk, the more follow-up testing is needed.

Did you know?

Clinical trials aren't just for people with advanced cancer.

Clinical trials can focus on all diagnoses and stages of disease, including:

- Preventing cancer from starting
- Treatment
- Delaying or preventing recurrence
- Improving quality of life

- Tests to monitor for the return of non–muscle-invasive disease in people of all risk levels include cystoscopy, imaging of the upper urinary tract, and imaging of the abdomen and pelvis. How often you should have these tests depends on your individual risk level.
- Follow-up urine cytology is recommended for people at average and high risk of the cancer returning.

5

Muscle-invasive bladder cancer

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If the tumor grows large enough to reach the thick layer of muscle in the bladder wall, it called muscle-invasive bladder cancer. Stage 2 and higher bladder cancers are muscle-invasive. All patients with localized, muscle-invasive disease should have surgery or chemoradiation therapy, if they are candidates for these treatments.

Stage 2

This stage means that the tumor has grown less than halfway through the muscle wall of the bladder (a T2a tumor) or more than halfway through (a T2b tumor). Cancer hasn't spread to lymph nodes or organs far from the bladder.

The answers to the following questions play an important role in choosing the best treatments for stage 2 bladder cancer:

- Are you healthy enough to undergo a major surgery to remove your bladder and other organs (radical cystectomy)?
- Can you tolerate chemotherapy with the drug cisplatin?

If you are healthy enough to have major surgery, you have both surgical and non-surgical treatment options, listed below. The best treatment option for you will depend on your individual circumstances.

- Chemotherapy followed by radical cystectomy
- Chemotherapy followed by partial cystectomy
- Chemotherapy and radiation therapy

- Radical cystectomy alone (if unable to receive cisplatin-based chemotherapy)

The treatment options listed above are explained next and shown in [Guide 5](#).

Chemotherapy followed by surgery

This option starts with chemotherapy that includes the drug cisplatin. Cisplatin has been shown to be the most effective chemotherapy medicine for treating bladder cancer. It may be too harsh for some people, especially people whose liver and kidneys don't work well. Liver and kidney function tends to decline with age. [See Guide 6](#) for the recommended cisplatin-based chemotherapy regimens to have before surgery.

After finishing chemotherapy to help shrink the tumor and kill any other microscopic deposits of cancer cells, surgery comes next. Most people will have a radical cystectomy. Radical cystectomy is the gold-standard surgery for muscle-invasive bladder cancer. Cisplatin-based chemotherapy followed by radical cystectomy is an NCCN "category 1" treatment option. This means that very high-quality research supports this treatment option.

A very small number of people (about 5 out of 100) may be able to have a partial (instead of a radical) cystectomy. You may be eligible for a partial cystectomy if:

- The tumor is at the top of the bladder and there are no fast-growing (high-grade) cells in other areas of the bladder lining
- The cancer is only in a small pouch sticking out from the bladder wall (called a diverticulum)
- You have other very serious health conditions that would prevent you from having a radical cystectomy

Depending on what the surgeon sees and learns first-hand during surgery, he or she may recommend radiation therapy to try to kill any remaining cancer cells. Reasons you may have radiation therapy include:

- The tumor was larger than expected
- The surgeon found cancer in lymph nodes
- The tumor started growing into the fatty tissue that surrounds the bladder

Chemoradiation

Chemotherapy and radiation therapy are used together to try to kill the cancer. When given together, both treatments work better than either does alone.

Chemoradiation is an NCCN category 1 treatment option. This means that very high-quality research supports this treatment option.

There are many different chemotherapies. When given with radiation, some chemotherapy medicines make it easier for radiation to kill cancer cells.

Guide 5. Stage 2: Treatment options for surgery candidates

Treatment options	What's first?		What's next?
Chemotherapy followed by radical cystectomy	Cisplatin-based chemotherapy (see Guide 6 for chemotherapy regimens)	➡	Radical cystectomy ➡ You may have radiation therapy
Chemotherapy followed by partial cystectomy <small>Not an option for most people</small>	Cisplatin-based chemotherapy (see Guide 6 for chemotherapy regimens)	➡	Partial cystectomy ➡ You may have radiation therapy
Chemoradiation	Radiation and chemotherapy given together (see Guide 7 for chemotherapy regimens)	➡	If the tumor is gone 2–3 months after treatment, begin follow-up care If the tumor is still there 2–3 months after treatment, treatment options include: <ul style="list-style-type: none"> • Intravesical BCG (if tumor is small enough) • Surgery to remove leftover tumor • Begin treatment for metastatic disease
Surgery alone	Radical cystectomy	➡	You may have one or both of these treatments: <ul style="list-style-type: none"> • Radiation therapy • Cisplatin-based chemotherapy

Medicines that make radiation work better are called “radiosensitizers.” See [Guide 7](#) below for the radiosensitizing chemotherapy regimens recommended by NCCN experts.

Like any treatment, chemoradiation has been shown to work better for certain people than for others. This may be a good option for you if [Guide 8](#) describes your cancer.

The size of the tumor should be checked 2 to 3 months after you’ve finished treatment. If the tumor is gone, you can begin follow-up care and monitoring

for the return of cancer. If the tumor is still there, there are 3 options:

- BCG therapy (if treatment shrunk the tumor enough so that it no longer invades the muscle wall of the bladder)
- Surgery to remove what’s left of the tumor
- Begin treatment for metastatic disease (see Part 6, *Treatment guide: Metastatic bladder cancer*)

Guide 6. Cisplatin-based chemotherapy given before or after surgery

Preferred regimens	What else do I need to know?
Dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin (DDMVAC)	NCCN experts recommend 3–4 cycles of this regimen. This regimen should be given with growth factor medication.
Gemcitabine and cisplatin	NCCN experts recommend 4 cycles of this regimen.

Other recommended regimen	What else do I need to know?
Cisplatin, methotrexate, and vinblastine (CMV)	NCCN experts recommend 3 cycles of this regimen.

Guide 7. Chemotherapy regimens for bladder-preserving chemoradiation

Preferred regimens	Other recommended regimen
<ul style="list-style-type: none"> • Cisplatin and fluorouracil (5-FU) • Cisplatin and paclitaxel (Taxol®) • 5-FU and mitomycin C • Cisplatin alone 	Low-dose gemcitabine (Gemzar®)

Radical cystectomy alone

This is an option for people who can't have cisplatin-based chemotherapy. You may not be able to have cisplatin if you have hearing loss, nerve damage, kidney problems, or if you are not able to do most activities. If you can't have cisplatin, you shouldn't have any chemotherapy before surgery.

Depending on what the surgeon sees and learns first-hand during surgery, you may also have radiation therapy to try to kill any remaining cancer cells. Reasons you may have radiation therapy include:

- The tumor was larger than expected
- The surgeon found cancer in lymph nodes
- The tumor started growing into the fatty tissue that surrounds the bladder

If you can't have (or don't want) a radical cystectomy

There are several reasons why you may not be able to have a radical cystectomy. If you have other serious health problems or you are not physically

able to do many day-to-day activities, surgery may not be an option for you. You may also simply not want to have a cystectomy.

There are three treatment options that don't involve removing the bladder. They are described next and shown in [Guide 9](#). Bladder cancer treatment that doesn't involve radical cystectomy is called "bladder-preserving."

Chemoradiation

This option allows you to keep your bladder. Chemotherapy and radiation therapy are used together to try to kill the cancer. When given together, chemotherapy and radiation therapy work better than either treatment does alone.

There are many different chemotherapy medicines. When given with radiation, some chemotherapy medicines make it easier for radiation to kill cancer cells. Medicines that make radiation work better are called "radiosensitizers." See Guide 7 on page 43 for the radiosensitizing chemotherapy regimens recommended by NCCN experts.

Guide 8. Best candidates for bladder-preserving chemoradiation

Best candidates for bladder preservation with chemoradiation

- The main (primary) tumor is smaller than 6 centimeters (about the length of a house key or a stick of gum).
- The tumor is not blocking the flow of urine from the kidneys into the bladder. If this happens, the kidneys can become enlarged because they are holding too much urine. This is called hydronephrosis.
- There are few, if any, areas of flat, fast-growing (high-grade) cancer cells on the inside lining of the bladder. This is called carcinoma in situ (CIS).
- The tumor can be all (or mostly) removed by TURBT.

Like any treatment, chemoradiation has been shown to work better for certain people than for others. This may be a good option for you if Guide 8 describes your cancer.

Radiation therapy alone

This treatment option is only for people who cannot have surgery or chemotherapy.

TURBT and possibly BCG therapy

If you cannot have (or don't want) surgery to remove your bladder, having another TURBT is an option for people with stage 2 bladder cancer. Compared to chemoradiation, there are less data supporting this treatment option in this setting. You may also have BCG therapy in addition to the TURBT.

Follow-up

The size of the tumor should be checked 2 to 3 months after you've finished treatment. If the tumor is gone, you can begin follow-up care and monitoring for the return of cancer. If your cancer responded and you were treated with BCG therapy, you should have maintenance BCG therapy.

If the tumor is still there, there are 4 options:

- Chemotherapy with one of the regimens in [Guide 6](#)
- Chemoradiation (only if you haven't already had any radiation therapy). [See Guide 7](#) on page 43 for the recommended chemotherapy regimens to use with radiation.
- TURBT to try to relieve symptoms caused by the tumor
- Begin supportive care

Next steps

See page 54 for recommendations for follow-up care and monitoring for the return of cancer.

Guide 9. Stage 2: Bladder-preserving treatment options

Treatment options	What's next?	What's next?
Chemoradiation		 If the tumor is gone , begin follow-up care. If you had intravesical BCG, continue maintenance BCG.
Radiation alone		 Check tumor size 2–3 months after treatment
TURBT and possibly BCG		 If the tumor is still there , options include: <ul style="list-style-type: none"> • Chemotherapy • Chemoradiation (if no prior radiation therapy) • TURBT to help with symptoms • Supportive care

Stage 3A

If you are healthy enough for surgery, there are both surgical and non-surgical treatment options. They include:

- Chemotherapy followed by radical cystectomy
- Radiation and chemotherapy (chemoradiation)
- Radical cystectomy alone

If you are not a candidate for surgery, the following treatments are options:

- Radiation and chemotherapy (chemoradiation)
- Radiation therapy alone

The treatment options listed above are explained next and shown in [Guide 10](#).

If you can have surgery

Chemotherapy followed by radical cystectomy

This treatment option starts with chemotherapy to try to shrink the tumor before surgery and to kill any microscopic cancer cells outside of the bladder.

You should have combination chemotherapy that includes the drug cisplatin. Cisplatin has been shown to be the most effective chemotherapy medicine for treating bladder cancer. It may be too harsh for some people, especially people whose liver and kidneys don't work well. [See Guide 6](#) on page 43 for recommended cisplatin-based chemotherapy regimens to have before surgery.

After finishing chemotherapy to help shrink the tumor, surgery (radical cystectomy) comes next.

Cisplatin-based chemotherapy followed by radical cystectomy is an NCCN category 1 treatment option. This means that very high-quality research supports this treatment option.

Depending on what the surgeon sees and learns first-hand during surgery, you may also have

radiation therapy to try to kill any remaining cancer cells. Reasons you may have radiation therapy include:

- The tumor was larger than expected
- The surgeon found cancer in lymph nodes
- The tumor started growing into the fatty tissue that surrounds the bladder

Radical cystectomy alone

Many people cannot tolerate cisplatin-based chemotherapy. In this case, surgery (radical cystectomy) alone is an option. Depending on what the surgeon sees and learns first-hand during surgery, you may also have radiation therapy to try to kill any remaining cancer cells. Reasons you may have radiation therapy include:

- The tumor was larger than expected
- The surgeon found cancer in lymph nodes
- The tumor started growing into the fatty tissue that surrounds the bladder

Chemoradiation

Chemotherapy and radiation therapy are used together to try to kill the cancer. When given together, chemotherapy and radiation work much better than either treatment does alone. **Chemoradiation is an NCCN category 1 treatment option. This means that very high-quality research supports this treatment option.**

There are many different chemotherapies. When given with radiation, some chemotherapy medicines make it easier for radiation to kill cancer cells. Medicines that make radiation work better are called "radiosensitizers." [See Guide 7](#) on page 43 for the radiosensitizing chemotherapy regimens recommended by NCCN experts.

Guide 10. Stage 3A treatment options

Treatment options if you **can and are willing to have surgery**

Treatment options		What's first?		What's next?
Chemotherapy followed by surgery	➡	Cisplatin-based chemotherapy (see Guide 6 for chemotherapy regimens)	➡	Radical cystectomy You may have radiation therapy
Surgery only	➡	Radical cystectomy	➡	You may have radiation therapy
Chemoradiation	➡	Radiation and chemotherapy given together (see Guide 7 for chemotherapy regimens)	➡	If the tumor is gone 2–3 months after treatment, begin follow-up care. If the tumor is still there 2–3 months after treatment, treatment options include: <ul style="list-style-type: none"> Intravesical BCG (if tumor is small enough) Surgery to remove leftover tumor Begin treatment for metastatic disease

Treatment options if you **can't or don't want to have surgery**

Treatment options		What's next?
Chemoradiation (see Guide 7 for chemotherapy regimens)	➡	If the tumor is gone 2–3 months after treatment, begin follow-up care. If the tumor is still there 2–3 months after treatment, treatment options include: <ul style="list-style-type: none"> Chemotherapy with one of the regimens in Guide 6 TURBT to relieve symptoms Begin supportive care
Radiation only	➡	

Like any treatment, chemoradiation has been shown to work better for certain people than for others. This may be a good option for you if [Guide 8](#) describes your cancer.

The size of the tumor should be checked 2 to 3 months after you've finished treatment. If the tumor is gone, you can begin follow-up care and monitoring for the return of cancer. If the tumor is still there, there are 3 treatment options:

- BCG therapy (if treatment succeeded at shrinking the tumor enough so that it no longer invades the muscle wall of the bladder)
- Surgery to remove what's left of the tumor
- Treatment for metastatic disease (see Part 6, *Treatment guide: Metastatic bladder cancer*)

If you can't have (or don't want) surgery

There are several reasons why you may not be able to have surgery. If you have other serious health problems or you are not physically able to do many day-to-day activities, surgery may not be an option for you.

Chemoradiation

This option allows you to keep your bladder. Chemotherapy and radiation therapy are used together to try to kill the cancer. When given together, chemotherapy and radiation therapy work much better than either treatment does alone.

There are many different chemotherapies. When given with radiation, some chemotherapy medicines make it easier for radiation to kill cancer cells. Medicines that make radiation therapy work better are called "radiosensitizers." [See Guide 7](#) on page 43 for the radiosensitizing chemotherapy regimens recommended by NCCN experts.

Like any treatment, chemoradiation has been shown to work better for certain people than for others. This may be a good option for you if [Guide 8](#) describes your cancer.

The size of the tumor should be checked 2 to 3 months after you've finished treatment. If the tumor is gone, you can begin follow-up care and monitoring for the return of cancer. If the tumor is still there, there are 3 options:

- Chemotherapy
- TURBT to try to relieve symptoms caused by the tumor
- Begin supportive care

Radiation therapy alone

Radiation therapy by itself does not work as well as chemotherapy and radiation therapy combined. This treatment option is only for people who cannot or choose not to have surgery or chemotherapy.

The size of the tumor should be checked 2 to 3 months after you've finished treatment. If the tumor is gone, you can begin follow-up care and monitoring for the return of cancer. If the tumor is still there, options include:

- TURBT to try to relieve symptoms caused by the tumor
- Chemotherapy may be considered
- Begin supportive care

Next steps

See page 54 for recommendations for follow-up care and monitoring for the return of cancer.

Stage 3B

The two primary (main) treatment options for stage 3B bladder cancer are systemic therapy and chemoradiation. More treatment may be needed depending on how well the primary treatment works.

Systemic therapy

This treatment option starts with systemic therapy to try to shrink the tumor as much as possible. If the treatment is successful, the tumor stage and size may go down. For this reason, you may hear it called “downstaging” systemic therapy.

The systemic therapy regimen you are treated with depends on whether you can tolerate chemotherapy

with the drug cisplatin. [Guide 11](#) lists the systemic therapy regimens to try first based on which drugs you can tolerate.

Two to three months after finishing systemic therapy, imaging tests are needed to see how the cancer responded to treatment. NCCN experts recommend CT of your chest, abdomen, and pelvis with contrast.

Complete response

If you had a complete response to the systemic therapy, having no further treatment is an option. In this case, you would start monitoring for the return of cancer.

Guide 11. Stages 3B and 4A: First systemic therapy options

What can you have?	Preferred regimens	Other recommended regimens
You can have cisplatin	<ul style="list-style-type: none"> Gemcitabine (Gemzar®) and cisplatin DDMVAC with growth factor support 	—
You cannot have cisplatin, but you can have carboplatin	<ul style="list-style-type: none"> Gemcitabine (Gemzar®) and carboplatin 	
You cannot have cisplatin and you have the PD-L1 biomarker	<ul style="list-style-type: none"> Gemcitabine (Gemzar®) and carboplatin (best choice if you can have carboplatin) Atezolizumab (Tecentriq®) Pembrolizumab (Keytruda®) 	<ul style="list-style-type: none"> Gemcitabine (Gemzar®) Gemcitabine (Gemzar®) and paclitaxel (Taxol®)
You cannot have any platinum-based chemotherapy	<ul style="list-style-type: none"> Atezolizumab (Tecentriq®) Pembrolizumab (Keytruda®) 	

Another option is to have more treatment to kill any remaining cancer cells. This is called consolidation therapy. The goal of consolidation therapy is to help “lock in” your good results from treatment with systemic therapy. Consolidation therapy is like a “final sweep” for leftover cancer cells still in the body.

Possible consolidation treatments you may have include:

- Surgery (radical cystectomy)
- Chemoradiation. [See Guide 7](#) on page 43 for the recommended chemotherapy regimens.

Partial response

If you had a partial response to the systemic therapy, more treatment is needed. Treatments you may have include:

- Surgery (radical cystectomy)
- Chemoradiation. [See Guide 7](#) on page 43 for the recommended chemotherapy regimens to be used with radiation if you’re not having a cystectomy.
- Begin treatment for metastatic disease. See Part 6, *Treatment guide: Metastatic bladder cancer*.

No response

If you had no response to systemic therapy and the cancer grew or spread, NCCN experts recommend beginning treatment for metastatic disease. See Part 6, *Treatment guide: Metastatic bladder cancer*.

Chemoradiation

Chemotherapy and radiation therapy are used together to try to kill the cancer. When given together, both treatments work better than either does alone.

This option allows you to keep your bladder. [See Guide 7](#) on page 43 for the radiosensitizing

chemotherapy regimens recommended by NCCN experts.

Two to three months after finishing chemoradiation, imaging tests are needed to see how the cancer responded to treatment. NCCN experts recommend CT of your chest, abdomen, and pelvis with contrast.

Complete response

If you have a complete response to chemoradiation, no more treatment is needed. You can begin follow-up care and monitoring for the return of cancer.

Partial response

If you have a partial response to chemoradiation, more treatment is needed. Next treatment options include:

- Intravesical BCG therapy (if treatment succeeded at shrinking the tumor enough so that it no longer invades the muscle wall of the bladder)
- Surgery to remove what’s left of the tumor
- Begin treatment for metastatic disease (see Part 6, *Treatment guide: Metastatic bladder cancer*)

No response

If your cancer didn’t respond to chemoradiation and the cancer grew or spread, NCCN experts recommend beginning treatment for metastatic disease. See Part 6, *Treatment guide: Metastatic bladder cancer*.

Next steps

See page 54 for recommendations for follow-up care and monitoring for the return of cancer.

Stage 4A

Some stage 4A bladder cancers have spread to lymph nodes called the “common iliacs,” which are beyond the pelvic region. This is “M1a” disease in the TNM staging system (see Part 2, *Staging bladder cancer*). If the cancer hasn’t spread to distant lymph nodes, it is called “M0” disease.

Treatment of all stage 4A bladder cancers starts out the same, but then differs based on whether there is cancer in distant lymph nodes. Treatment options are described next and shown in [Guide 12](#).

Guide 12. Stage 4A bladder cancer: treatment options

Cancer **hasn’t** spread to distant lymph nodes or organs

Treatment options		Result of treatment and next steps
Option 1: Systemic therapy only	 Follow-up testing	<p>If the tumor is gone, next treatment options include:</p> <ul style="list-style-type: none"> Consolidation systemic therapy Chemoradiation (if you didn’t already have radiation) Radiation therapy if you didn’t have full amount Surgery (radical cystectomy)
Option 2: Chemoradiation	 Follow-up testing	<p>If the tumor is still there, next treatment options include:</p> <ul style="list-style-type: none"> Systemic therapy Chemoradiation (if you didn’t already have radiation) Try a different systemic therapy regimen Surgery (radical cystectomy)

Cancer **has** spread to distant lymph nodes, but not to distant organs

Treatment options		Result of treatment and next steps
Option 1: Systemic therapy only	 Follow-up testing	<p>If the cancer is gone, next treatment options include:</p> <ul style="list-style-type: none"> A boost of radiation therapy Surgery (radical cystectomy)
Option 2: Chemoradiation	 Follow-up testing	<p>If the cancer hasn’t improved or has gotten worse, begin treatment for persistent disease (see page 56).</p>

the cancer responded to treatment. Testing is recommended after 2 to 3 cycles of systemic therapy, or 2 to 3 months after finishing chemotherapy and radiation.

NCCN experts recommend the following tests:

- Cystoscopy
- Bimanual examination under anesthesia
- TURBT
- Imaging tests of your abdomen and pelvis

Next treatment(s)

The next treatment options depend on whether there is cancer in distant lymph nodes and whether you had a good response to primary treatment.

Cancer hasn't spread to distant lymph nodes (M0)

If you had a complete response to treatment with either systemic therapy or chemoradiation and the tumor is gone, next treatment options include:

- Systemic therapy to kill any cancer cells that may still be in the body. This is called consolidation systemic therapy. [See Guide 11](#) for recommended systemic therapy regimens.
- Radiation and chemotherapy. This option is only for people who haven't had any radiation therapy. [See Guide 7](#) on page 43 for recommended chemotherapy regimens to be used with radiation.
- If you were previously treated with radiation but at a lower dose, NCCN experts recommend that you have more radiation to get the full amount of radiation you can have.
- Surgery (radical cystectomy) if the tumor is small enough

If testing shows that the tumor is still there, there are several treatment options:

- Systemic therapy with one of the regimens in [Guide 11](#)
- Radiation and chemotherapy. This option is only for people who haven't had any radiation therapy. [See Guide 7](#) on page 43 for recommended chemotherapy regimens to be used with radiation.
- Trying a different systemic therapy regimen. [See Guide 13](#) for systemic therapy regimens to try next.
- Surgery (radical cystectomy) if the tumor is small enough

Cancer has spread to distant lymph nodes (M1a)

If you had a complete response to treatment with either systemic therapy or chemoradiation and the tumor is gone, next treatment options include:

- More doses of radiation directed at where the tumor was. The goal is to lower the risk of the cancer coming back. This is called a "boost" of radiation.
- Surgery (radical cystectomy)

If testing shows that the cancer has stayed the same or gotten worse, this is called persistent disease. See "If cancer persists, returns, or spreads" on page 56.

Next steps

Recommendations for follow-up care and monitoring for the return of cancer are explained in the next section.

Guide 13. Stages 3B and 4A: Next systemic therapy options

Prior treatment	Preferred regimens	Other recommended regimens
You were treated with platinum-based chemotherapy	<p>Preferred regimen: Pembrolizumab (Keytruda®)</p> <p>Alternative preferred regimens:</p> <ul style="list-style-type: none"> • Atezolizumab (Tecentriq®) • Nivolumab (Opdivo®) • Durvalumab (IMFINZI™) • Avelumab (Bavencio®) • Erdafitinib (BALVERSA™) - only for patients with FGFR3 or FGFR2 mutations 	<ul style="list-style-type: none"> • Albumin-bound paclitaxel (Abraxane®) • Paclitaxel (Taxol®) • Docetaxel (Taxotere®) • Gemcitabine (Gemzar®) • Pemetrexed (Alimta®)
You were treated with a checkpoint inhibitor and cannot have cisplatin	Gemcitabine (Gemzar®) and carboplatin	
You were treated with a checkpoint inhibitor and can have cisplatin	<ul style="list-style-type: none"> • Gemcitabine (Gemzar®) and cisplatin • DDMVAC with growth factor support 	

Follow-up care

When you have finished treatment, the next phase of cancer care begins. This is the surveillance phase. During this time it is important to have testing to monitor for the return of cancer. The specific tests you should have—and how often you should have them—depends on whether your bladder was removed.

Your bladder was removed

Follow-up after a radical cystectomy should include imaging studies, urine and blood tests, and liver and kidney function testing. Kidney function tests include electrolytes and creatinine.

Liver function tests include:

- Aspartate aminotransferase (AST)
- Alanine aminotransferase (ALT)
- Bilirubin
- Alkaline phosphatase

After the first year of follow-up care, patients should also have their vitamin B12 level tested once a year. Urethral wash cytology is recommended during the first two years of follow-up care for patients with high-risk disease who have an ileal conduit or a continent urinary reservoir (Indiana pouch).

Guide 14. Follow-up care after radical cystectomy

Test	Year 1	Year 2	Year 3	Year 4	Year 5	Years 6–10	After 10 Years
Imaging	Every 3–6 months: <ul style="list-style-type: none"> • CT urogram or MR urogram • Chest x-ray or chest CT 		Once a year: <ul style="list-style-type: none"> • CT or MRI of abdomen and pelvis • Chest x-ray or chest CT 			Once a year: Ultrasound of the kidneys	As directed by your doctor based on symptoms
	PET/CT only if metastatic disease suspected						
Blood tests	Every 3–6 months: <ul style="list-style-type: none"> • Kidney function testing • Liver function testing • CBC and CMP (if you had chemotherapy) 		Once a year: <ul style="list-style-type: none"> • Kidney function testing • Liver function testing • Vitamin B₁₂ testing 			Once a year: Vitamin B ₁₂ testing	
Urine tests	Every 6–12 months: <ul style="list-style-type: none"> • Urine cytology • Urethral wash cytology for people with high-risk disease who have an ileal conduit or a continent urinary reservoir (Indiana pouch) 					• Urine cytology as directed by your doctor • Urethral wash cytology as directed by your doctor	

Follow-up after a partial cystectomy is similar to that for a radical cystectomy. One difference is that after partial cystectomy, cytology and cystoscopy are recommended to look for signs that cancer has returned to the bladder.

See Guide 14 for the recommended schedule of follow-up testing after radical cystectomy.

You have your bladder

For patients who have a preserved bladder, there is a risk that cancer will return to the bladder, to somewhere else in the urinary tract, or to areas far from the bladder.

Follow-up after bladder-preserving treatment should include cystoscopy, imaging studies, urine and blood tests, and liver and kidney function testing. Kidney function tests include electrolytes and creatinine. Liver function tests include:

- Aspartate aminotransferase (AST)
- Alanine aminotransferase (ALT)
- Bilirubin
- Alkaline phosphatase

See Guide 15 for the recommended schedule of follow-up testing after bladder-preserving treatment.

Guide 15. Follow-up care after bladder-preserving treatment

Test	Year 1	Year 2	Year 3	Year 4	Year 5	Years 6–10	After 10 Years
Cystoscopy	Every 3 months		Every 6 months		Once a year		As directed by your doctor
Imaging	Every 3–6 months: <ul style="list-style-type: none"> • CT urogram or MR urogram • Chest x-ray or chest CT 		Once a year: <ul style="list-style-type: none"> • CT or MRI of abdomen and pelvis • Chest x-ray or chest CT 	As directed by your doctor			
	PET/CT only if metastatic disease suspected						
Blood tests	Every 3–6 months: <ul style="list-style-type: none"> • Kidney function testing • Liver function testing • CBC and CMP (if you had chemotherapy) 			<ul style="list-style-type: none"> • Kidney function testing as directed by your doctor • Liver function testing as directed by your doctor 			
Urine tests	Every 6–12 months: <ul style="list-style-type: none"> • Urine cytology 			<ul style="list-style-type: none"> • Urine cytology as directed by your doctor 			

If cancer persists, returns, or spreads

Treating cancer that returns after treatment depends in part on whether your bladder was removed.

You have your bladder

Cancer hasn't responded to treatment (persistent disease)

In people with a preserved bladder, the treatment options for cancer that hasn't responded to treatment are the same as cancer that returned to the bladder (or nearby). Treatment options depend on the size of the tumor and are explained next.

Cancer returned to the bladder (or nearby)

If cancer returns to the bladder (or nearby), it is called a local recurrence. It should be treated as a new cancer, while taking into account the size of the tumor and treatments you've already had.

Non-muscle-invasive tumors (Tis, Ta, T1 tumors) are usually treated with BCG therapy or radical cystectomy. If BCG therapy is used and doesn't work, radical cystectomy is recommended. If you are not a candidate for surgery, options include:

- Chemoradiation (only if you haven't had any prior radiation therapy). [See Guide 7](#) on page 43 for the recommended chemotherapy regimens to be used with radiation.
- Switching from BCG to a different intravesical medicine
- Joining a clinical trial

Muscle-invasive tumors (T2 and above) are usually treated in one of four ways:

- **Radical cystectomy.** This may not be possible if you have undergone a full course of EBRT and have a large tumor. In this case, best supportive care and TURBT to help

relieve symptoms caused by the tumor are recommended.

- **Chemoradiation.** This is an option for people who haven't had any prior radiation therapy. [See Guide 7](#) on page 43 for the recommended chemotherapy regimens to be used with radiation.
- **Palliative TURBT.** This is an option for people who have undergone a full course of EBRT and are not candidates for surgery. TURBT can be done to help relieve symptoms caused by the tumor. This is considered a palliative TURBT, because the goal is to make you more comfortable, not to cure the cancer.
- **Supportive care.** Supportive care aims to improve your quality of life. It includes care for health issues caused by cancer or its treatment. Supportive care is important for everyone, not just people at the end of life.

Follow-up urine cytology found cancer

If follow-up urine cytology suggest cancer has returned, but cystoscopy, examination under anesthesia, and biopsies of nearby areas do not, more testing should be done. Recommended testing includes:

- Retrograde selective washings of the upper urinary tract. This means that fluid will be put into the kidneys and ureters and then removed and tested for cancer cells. If cancer cells are found, treatment of the upper urinary tract is needed.
- A biopsy of the part of the urethra closest to the inside of the body. This is called the proximal urethra. In men, the proximal (or prostatic) urethra crosses through the prostate gland. If the biopsy finds cancer cells, treatment of the prostate is needed.

Your bladder was removed

If your bladder was removed and cancer returned to the bladder area or metastasized, treatment options include:

Systemic therapy. Regimens to try first (called “first-line” regimens) are presented in [Guide 11](#) on page 49; regimens to try if first-line systemic therapy fails (called “second-line” regimens) are shown in [Guide 13](#) on page 53.

Chemoradiation (only if you haven’t had any radiation therapy to the area). Chemotherapy is sometimes combined with radiation to treat metastases or cancer that has returned to the bladder area after radical cystectomy. However, a lower dose of radiation is used compared to radiation given with chemotherapy as the primary (main) treatment option.

In this situation, the preferred chemotherapy regimen to be used with radiation is cisplatin. Other recommended regimens include:

- Docetaxel or paclitaxel
- 5-FU with or without mitomycin C
- Low-dose gemcitabine

Radiation alone. This option may be helpful if the cancer hasn’t spread far from the bladder or if the tumor is causing symptoms.

Review

- If a bladder tumor grows large enough to reach the thick layer of muscle in the bladder wall, it is called muscle-invasive bladder cancer. Stage 2 and higher bladder cancers are muscle-invasive.
- In people healthy enough for surgery, the treatment options for stage 2 and 3A bladder cancer that are most strongly supported by research are cisplatin-based chemotherapy followed by radical cystectomy, and chemoradiation.
- The primary (main) treatment options for stage 3B and 4A bladder cancer are systemic therapy and chemoradiation. More treatment may be needed depending on how well the primary treatment works. For stage 4A, next treatment(s) also depend on whether cancer has spread to lymph nodes far from the bladder.
- Follow-up testing after treatment for muscle-invasive disease includes imaging tests, blood tests, and urine tests. For patients who have their bladder, cystoscopy is also needed to look for signs that cancer has returned to the bladder.

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Metastatic bladder cancer

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If cancer spreads to areas far from the bladder, it is called metastatic cancer. If it has already metastasized by the time you are diagnosed, it is stage 4B bladder cancer. Treatment of metastatic bladder cancer is focused on helping you live as normally and as comfortably as possible, for as long as possible.

First steps

If your doctor suspects that cancer has spread beyond the pelvic region, he or she will likely order tests to find out how many metastases there are and where they are in the body. The tests your doctor may order include:

- A bone scan (if your doctor thinks there may be cancer in your bones based on your symptoms or results of laboratory tests)
- CT of your chest
- MRI of your brain (if you have certain symptoms or a high-risk tumor type). If you can't have an MRI, CT with IV contrast is recommended instead.
- A kidney function test called the estimated glomerular filtration rate (eGFR). The purpose of this test is to see if you can tolerate a chemotherapy drug called cisplatin.
- A biopsy of any suspicious areas
- Biomarker testing for PD-L1 expression and FGFR inhibition. See Part 1, *Bladder cancer basics* for more information on these tests. The purpose is to find out if you have any tumor markers that may mean you are eligible for treatment with certain targeted therapies.



SNAPSHOT

Metastatic bladder cancer

- ✓ If cancer spreads to organs far from the bladder, it is called metastatic cancer.
- ✓ If it has already metastasized by the time you are diagnosed, it is stage 4B bladder cancer.
- ✓ About 4 out of 100 people will have metastatic disease at the time of diagnosis.
- ✓ The main treatment is systemic therapy (chemotherapy, targeted therapy, and immunotherapy).
- ✓ A small number of people may benefit from surgery to remove metastases.

Systemic therapy

The main treatment for metastatic bladder cancer is systemic therapy. Systemic therapy includes chemotherapy, targeted therapy, and immunotherapy medicines. In order to determine which systemic therapy medicines are 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.

Regimens to try first

NCCN experts recommend starting with one of the systemic therapy regimens in [Guide 16](#). They are called “first-line” regimens because they have the best chance of working and should therefore be used

first. There are other regimens not listed in Guide 16 that may be useful in certain circumstances, depending on the treatment you’ve already received.

Follow-up

Your doctor will want to see how well the chemotherapy is working after 2 to 3 cycles of treatment. If the cancer has stayed the same or improved, treatment is usually continued for 2 more cycles. If the cancer doesn’t respond 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.

Guide 16. Metastatic bladder cancer: First systemic therapy options

What can you have?	Preferred regimens	Other recommended regimens
You can have cisplatin	<ul style="list-style-type: none"> Gemcitabine (Gemzar®) and cisplatin DDMVAC with growth factor support 	—
You cannot have cisplatin, but you can have carboplatin	<ul style="list-style-type: none"> Gemcitabine (Gemzar®) and carboplatin 	
You cannot have cisplatin and you have the PD-L1 biomarker	<ul style="list-style-type: none"> Gemcitabine (Gemzar®) and carboplatin (best choice if you can have carboplatin) Atezolizumab (Tecentriq®) Pembrolizumab (Keytruda®) 	<ul style="list-style-type: none"> Gemcitabine (Gemzar®) Gemcitabine (Gemzar®) and paclitaxel (Taxol®)
You cannot have any platinum-based chemotherapy	<ul style="list-style-type: none"> Atezolizumab (Tecentriq®) Pembrolizumab (Keytruda®) 	

Regimens to try next

If cancer progresses after first-line systemic therapy, there are other regimens you can try next. These are called “second-line” or “subsequent-line” regimens.

Options for second-line therapy depend on which systemic therapy you were treated with first. If you were treated with platinum-based chemotherapy (cisplatin or carboplatin) more than 12 months ago, you may be able to have it again (if you can still tolerate it).

See Guide 17 for the second-line systemic therapy regimens recommended by NCCN experts.

There are other regimens not listed in Guide 17 that may be useful in certain circumstances, depending on the treatment you’ve already received.

Guide 17. Metastatic bladder cancer: Next systemic therapy options

Previous treatment	Preferred regimens	Other recommended regimens
You had platinum-based chemotherapy	<p>Preferred regimen:</p> <ul style="list-style-type: none"> Pembrolizumab (Keytruda®) <p>Alternative preferred regimens:</p> <ul style="list-style-type: none"> Atezolizumab (Tecentriq®) Nivolumab (Opdivo®) Durvalumab (IMFINZI™) Avelumab (Bavencio®) Erdafitinib (BALVERSA™) - <i>for patients with FGFR3 or FGFR2 mutations</i> 	<ul style="list-style-type: none"> Albumin-bound paclitaxel (Abraxane®) Paclitaxel (Taxol®) Docetaxel (Taxotere®) Gemcitabine (Gemzar®) Pemetrexed (Alimta®)
You were treated with a checkpoint inhibitor and you CANNOT have cisplatin	Gemcitabine (Gemzar®) and carboplatin	
You were treated with a checkpoint inhibitor and you CAN have cisplatin	<ul style="list-style-type: none"> Gemcitabine (Gemzar®) and cisplatin DDMVAC with growth factor support 	

**SNAPSHOT**

Systemic therapy for metastatic bladder cancer

Platinum-based chemotherapy

cisplatin

carboplatin

- The standard of care for metastatic bladder cancer
- Given in combination with other chemotherapy agents
- Cisplatin and carboplatin are platinum-based chemotherapies
- Cisplatin is the stronger drug in terms of response and side effects
- This type of chemotherapy (especially cisplatin) can damage the kidneys
- Many people can't have cisplatin because their kidneys don't work well or because of other health issues.

Checkpoint inhibitors

pembrolizumab (Keytruda®)

atezolizumab (Tecentriq®)

nivolumab (Opdivo®)

durvalumab (IMFINZI™)

avelumab (Bavencio®)

- Checkpoint inhibitors are a newer treatment option for locally advanced and metastatic bladder cancer
- Can be used for bladder cancer that progresses or metastasizes after platinum-based chemotherapy
- Some can also be used as first-line therapy for people with the PD-L1 biomarker who can't have cisplatin, and for people who can't have any platinum-based chemotherapy

FGFR inhibitor

erdafitinib (BALVERSA™)

- New treatment option for some people with *FGFR2* or *FGFR3* mutations
- For people with locally advanced or metastatic disease who have progressed on platinum-based chemotherapy
- Given as a once-daily pill

Other systemic therapies

- There are other systemic therapy regimens that may be helpful.
- NCCN experts recommend joining a clinical trial if there is one available to you.

Other treatments

Surgery for metastases

After systemic therapy, a small number of people may benefit from surgery to remove metastases. Surgery is most likely to help you if:

- Your cancer doesn't seem to be spreading quickly
- Your cancer responded well to systemic therapy
- The metastases are in only one area (only in the liver, for example)
- The metastases are in favorable areas, such as the lungs or lymph nodes, and can be removed by surgery

Clinical trials

NCCN experts believe that the best management of all patients with cancer is in a clinical trial. Joining a clinical trial is strongly recommended for people with bladder cancer who have not responded to first- and second-line systemic therapy.

Supportive care

Supportive care aims to improve your quality of life. It includes care for health issues caused by cancer or cancer treatment. It is also sometimes called palliative care.

Palliative care is important for everyone with cancer, not just people at the end of life. In fact, it has been shown to extend and enhance life for people with metastatic bladder cancer.



Which chemotherapy drugs can I have?

Your ability to do day-to-day tasks and activities is called your “performance status.” Your performance status and overall health play a major role in selecting the best chemotherapy regimens for you. People with liver or kidney problems, or other serious health issues, should receive less harsh chemotherapy medicines. Some people may not be able to tolerate any chemotherapy medicines.

Side effects

Treatment of bladder cancer can cause unwanted changes to your body and mind, called side effects. Some side effects can be harmful to your health, while others are just unpleasant. The effects of treatment depend on many factors, especially the treatment type (radiation versus chemotherapy, for example) and the length or dose of the treatment. Side effects can last for years; some may never go away.

Treatment of bladder cancer can cause sexual problems, including 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. Men may also experience difficulty getting or keeping an erection (erectile dysfunction) and ejaculation without semen (“dry ejaculation”). Women may experience pain during sex, vaginal dryness, and trouble achieving orgasm.

Many people find that they have trouble controlling the flow of urine after bladder cancer treatment. This is called urinary incontinence. In other words, urine might come out when you don't want it or expect it to, including during sex.

Sexual dysfunction and urinary incontinence are only two examples of side effects. Ask your treatment team for a complete list of short- and long-term side effects and information on how to manage them. Many side effects can be managed; some may even be preventable.

Review

- The main treatment for metastatic bladder cancer is systemic therapy. The main systemic therapies used are platinum-based combination chemotherapy, immunotherapy (checkpoint inhibitors) and a targeted therapy (FGFR inhibitor).
- A small number of people may benefit from surgery to remove metastases.
- Joining a clinical trial is encouraged for all patients with bladder cancer, and is strongly recommended by NCCN for people with metastatic bladder cancer that has not responded to systemic therapy.

“

It is often hard to talk to family due to the fact you know they hurt for you. Talking to people with the same issues and getting information received has been amazing. I am atypical, being diagnosed with bladder cancer at age 26.

– Tracy, age 34

8-year bladder cancer survivor

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Making treatment decisions

-
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 - 66 Questions to ask your doctors**
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Having cancer is very stressful. There is a lot to learn in what feels like a short time. This chapter can help you make decisions that reflect your beliefs, wishes, and values.

It's your choice

The role patients want in choosing their treatment differs. You may feel uneasy about making treatment decisions. This may be due to a high level of stress. Stress, pain, and medications can limit your ability to make good decisions. You may feel uneasy because you don't know much about cancer. You've never heard the words used to describe cancer, tests, or treatments. You may also simply think that your judgment isn't any better than your doctors'.

Letting others decide which option is best may make you feel more at ease. But, whom do you want to make the decisions? You may rely on your doctors alone to make the right decisions. However, your doctors may not tell you which to choose if you have more than one good option. You can also have loved ones help. They can gather information, speak on your behalf, and share in decision-making with your doctors. Even if others decide which treatment you will receive, you still must agree by signing a consent form.

On the other hand, you may want to take the lead or share in decision-making. Most patients do. In shared decision-making, you and your doctors share information, weigh the options, and agree on a treatment plan. Your doctors know the science behind your plan but you know your concerns and goals. By working together, you are likely to get a higher quality of care and be more satisfied. You'll likely get the treatment you want, at the place you want, and by the doctors you want.

Questions to ask your doctors

You may meet with experts from different fields of medicine. Try to talk with each expert. Prepare questions before your visit and ask questions if the person isn't clear. You can also record your talks and get copies of your medical records. It may be helpful to have your spouse, partner, or a friend with you at these visits. They can help to ask questions and remember what was said. Below are some suggested questions to ask.

Figure 8. Informed consent form

Even if others decide which treatment you will receive, you still have to agree by signing a consent form.



What's my diagnosis and prognosis?

Cancer can greatly differ even when people have a tumor in the same organ. Your doctor should clearly explain the type of cancer you have. This is your diagnosis. Your doctor should also be able to tell you how he or she expects it to respond to treatment. This is your prognosis.

1. Where did the cancer start?
 2. Is this cancer common?
 3. What is the cancer stage? Does this stage mean the cancer has spread far?
 4. Is this a fast- or slow-growing cancer?
 5. What other test results are important to know?
 6. How often are these tests wrong?
 7. Would you give me a copy of the pathology report and other test results?
 8. How likely is it that I'll be cancer-free after treatment?
-
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-
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-
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-
-
-

What are my options?

There is no single treatment practice that is best for all patients. There is often more than one treatment option along with clinical trial options. Your doctor will review your test results and recommend treatment options.

1. What will happen if I do nothing?
 2. Can I just carefully monitor the cancer?
 3. Do you consult the NCCN Clinical Practice Guidelines in Oncology® when considering treatment options?
 4. Are you suggesting options other than what NCCN recommends? If yes, why? What are these other options based on?
 5. Do your suggested options include clinical trials? Please explain why or why not.
 6. How do my age, health, and other factors affect my options?
 7. Which option is proven to work best? Which options lack scientific proof?
 8. What are the benefits of each option? Does any option offer a cure? Are my chances any better for one option than another? Less time-consuming? Less expensive?
 9. What are the risks of each option? What are possible complications? What are the rare and common side effects? Short-lived and long-lasting side effects? Serious or mild side effects? Other risks?
 10. What can be done to prevent or relieve the side effects of treatment?
 11. What are my chances that the cancer will return?
 12. What if I continue smoking? Stop smoking?
 13. What is the likely financial burden that I will bear as a result of this treatment?
-
-
-

Weighing your options

Deciding which option is best can be hard. Doctors from different fields of medicine may have different opinions on which option is best for you. This can be very confusing. Your spouse or partner may disagree with which option you want. This can be stressful. In some cases, one option hasn't been shown to work better than another, so science isn't helpful. Some ways to decide on treatment are discussed next.

Second opinion

After finding out you have cancer, it is normal to want to start treatment as soon as possible. While cancer can't be ignored, there is time to have another doctor 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.

Getting a second opinion doesn't mean you don't trust the first doctor. In fact, most doctors who are diagnosed with cancer will see more than one doctor before beginning treatment. What's more, some health plans require a second opinion. If your health plan doesn't cover the cost of a second opinion, you have the choice of paying for it yourself.

If the two opinions are the same, you may feel better about the treatment you accept to have. If the two opinions differ, think about getting a third opinion. Choosing your cancer treatment is a very important decision. It can affect your length and quality of life.

Support groups

Besides talking to health experts, it may help to talk to patients who have walked in your shoes. Support groups often consist of people at different stages of treatment. Some may be in the process of deciding while others may be finished with treatment. At support groups, you can ask questions and hear about the experiences of other people with bladder cancer. Both in-person and virtual support groups exist for bladder cancer.

Compare benefits and downsides

Every option has benefits and downsides. Consider these when deciding which option is best for you. Talking to others can help identify benefits and downsides you haven't thought of.

Websites

American Bladder Cancer Society

<https://bladdercancersupport.org>

Bladder Cancer Advocacy Network

<https://www.bcan.org>

National Cancer Institute

<https://www.cancer.gov/types/bladder>

NCCN

www.nccn.org/patients

Urology Care Foundation

<https://www.urologyhealth.org>

U.S. National Library of Medicine Clinical Trials Database

www.clinicaltrials.gov

Review

- Shared decision-making is a process in which you and your doctors plan treatment together.
- Asking your doctors questions is vital to getting the information you need to make informed decisions.
- Getting a second opinion, attending support groups, and comparing pros and cons may help you decide which treatment is best for you.



Words to know

Bacillus Calmette Guérin (BCG)

An immunotherapy medicine put directly in the bladder to treat bladder cancer.

biomarker

Any molecule in your body that can be measured to assess your health. Usually identified by a test done on your tumor tissue or a blood test.

biopsy

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

bone scan

A test that makes pictures of bones to assess for health problems.

cancer grade

A rating of how much the cancer cells look like normal cells under a microscope and how aggressive the cancer is.

cancer stage

A rating of the outlook of a cancer based on its growth and spread.

carcinoma in situ (CIS)

Flat, high-grade (fast-growing) tumors.

chemoradiation

Cancer treatment with both chemotherapy and radiation therapy.

chemotherapy

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

clinical stage

The rating of the extent of cancer before surgery.

clinical trials

A type of research that assesses how well health tests or treatments work in people.

computed tomography (CT)

A test that uses x-rays from many angles to make a picture of the insides of the body.

complete blood count (CBC)

A common blood test that provides information about the numbers and kinds of cells in the blood, especially red blood cells, white blood cells, and platelets.

computed tomography urogram (CTU)

An imaging method that uses x-rays to create detailed pictures of the kidneys, ureters, and bladder.

consolidation therapy

A treatment given after the cancer is gone in order to kill any last cancer cells that may be hiding in the body. Also called intensification therapy and postremission therapy.

continent urinary reservoir

A type of urinary diversion in which a piece of intestine is used to make a small reservoir in the wall of the abdomen. A catheter is used to drain urine from the reservoir. Also called an Indiana pouch and a continent catheterizable diversion.

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 the doctor's regular office in a procedure room.

dose-dense chemotherapy

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

dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin (DDMVAC)

A chemotherapy regimen used to treat bladder cancer.

examination under anesthesia (EUA)

An examination of a specific area of the body while the patient is under general anesthesia.

external beam radiation therapy (EBRT)

A cancer treatment with radiation delivered from a machine outside the body.

glomerular filtration rate (GFR)

The flow rate of filtered fluid through the kidneys to assess the function of the kidneys before giving cisplatin-based chemotherapy.

growth factor

A substance that helps new blood cells to be made.

Used to help the blood cells recover between rounds of chemotherapy.

Words to know

hematuria

The presence of blood in urine.

hydronephrosis

Abnormal enlargement (swelling) of a kidney caused by a build-up of urine. In cancer, this can be caused by an obstruction from the tumor growth.

ileal conduit

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

immunotherapy

Treatment with drugs that help the body's immune system find and destroy cancer cells.

instillation

A method used to slowly put liquid into the body.

intravesical therapy

A treatment using medicine put directly into the bladder.

lamina propria

A layer of connective tissue within the wall of the urinary tract.

locally advanced cancer

Cancer that has spread from the first site to nearby tissue or lymph nodes.

local therapy

A treatment that is given to a specific area or organ of the body.

magnetic resonance imaging (MRI)

An imaging method that uses radio waves and powerful magnets to make pictures of the insides of the body.

magnetic resonance urogram (MRU)

An imaging method that uses magnetic waves to create detailed pictures of the kidneys, ureters, and bladder.

medical history

A report of all your health events and medications.

muscularis propria

The third layer of the wall of the urinary tract. Also called the detrusor muscle.

mutation

An abnormal change in the coded instructions within cells.

neobladder

A type of urinary diversion in which a piece of small intestine is made into a hollow pouch that can hold and drain urine.

observation

A period of testing for changes in cancer status while not receiving treatment.

pathologic stage

A rating of the extent of cancer based on tests given after surgery to treat the primary tumor.

positron emission tomography (PET)

A test that uses radioactive material to see the shape and function of body parts.

primary treatment

The main treatment used to rid the body of cancer.

radiation therapy

A treatment that uses intense energy to kill cancer cells.

radical cystectomy

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

radiosensitization

The use of a drug that makes tumor cells more sensitive to radiation therapy.

radiosensitizing agent

Any substance that makes tumor cells easier to kill with radiation therapy. Some radiosensitizing agents are being studied in the treatment of cancer. Also called radiosensitizer.

recurrence

The return of cancer after a cancer-free period.

supportive care

Health care that includes symptom relief but not cancer treatment. Also called palliative care.

surveillance

Testing that is done after treatment ends to look for new tumors.

systemic therapy

A type of treatment that works throughout the body.

targeted therapy

A cancer treatment that may target and attack specific types of cancer cells.

Words to know

transurethral resection of the bladder tumor

(TURBT)

A procedure to remove bladder tumors via the urethra.

Determines the tumor stage of bladder cancer.

ureter

A long, tube-shaped structure that carries urine from the kidneys to the bladder.

ureteroscopy

A procedure that allows a doctor to see inside the kidney and ureter using a special tool called a uteroscope. The uteroscope is inserted into the urethra and then guided through the bladder, ureter, and into the kidney.

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 disease.

urothelium

The stretchy lining of the organs of the urinary tract. This includes the kidneys, ureters, bladder, and urethra.

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NCCN Cancer Centers

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

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
800.999.5465
nebraskamed.com/cancer

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

City of Hope National Medical Center
Los Angeles, California
800.826.4673
cityofhope.org

Dana-Farber/Brigham and
Women's Cancer Center
Massachusetts General Hospital
Cancer Center
Boston, Massachusetts
877.332.4294
dfbwcc.org
massgeneral.org/cancer

Duke Cancer Institute
Durham, North Carolina
888.275.3853
dukecancerinstitute.org

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427
foxchase.org

Huntsman Cancer Institute
at the University of Utah
Salt Lake City, Utah
877.585.0303
huntsmancancer.org

Fred Hutchinson Cancer
Research Center/Seattle
Cancer Care Alliance
Seattle, Washington
206.288.7222 • seattlecca.org
206.667.5000 • fredhutch.org

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

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

Mayo Clinic Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
800.446.2279 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
www.mayoclinic.org/cancercenter

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

Moffitt Cancer Center
Tampa, Florida
800.456.3434
moffitt.org

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

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

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
888.226.4343 • stjude.org
901.683.0055 • westclinic.com

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

UC San Diego Moores Cancer Center
La Jolla, California
858.657.7000
cancer.ucsd.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
mcancer.org

The University of Texas
MD Anderson Cancer Center
Houston, Texas
800.392.1611
mdanderson.org

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

Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
800.811.8480
vicc.org

Yale Cancer Center/
Smilow Cancer Hospital
New Haven, Connecticut
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