

TREATMENT UPDATE:
Bladder Cancer

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Treatment Update: Bladder Cancer

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Bladder cancer makes up about 4 percent of cancers in the United States. It is more common in men than in women.

About 95 percent of bladder cancers are classified as “urothelial carcinoma” (previously called transitional cell carcinoma), meaning that the cancer (carcinoma) arises mostly from the cells that line the inside of the bladder. Urothelial carcinomas can also arise from cells in other places along the urinary tract, including the inner lining of the kidneys, the ureters and the urethra.

In approximately 70 percent of urothelial carcinomas, the cancer is contained within the superficial lining of the bladder. The remaining cases are classified as “muscle invasive,” meaning that the cancer cells have spread beyond the inner lining of the bladder into the muscle layer or has spread outside the bladder.



Treatment Options

The course of treatment for bladder cancer is often determined after consultations with a urologist, a medical oncologist and a radiation oncologist. Each doctor brings a perspective unique to their specialty.

Non-invasive bladder cancer

If the cancer cells are non-invasive (contained within the lining of the bladder), the treatment approach is decided with a number of factors in mind, including what was seen on the diagnostic imaging tests and other health issues the person may have.

Treatment approaches for non-invasive bladder cancer are typically a combination of the following:

- **Transurethral resection of bladder tumor (TURBT).** A small electrified wire loop is passed through a cystoscope into the bladder and is used to remove the tumor.
- **Partial cystectomy.** The portion of the bladder that contains cancer cells is removed.
- **Bacille Calmette-Guerin (BCG).** BCG is an intravesical (delivered directly into the bladder) therapy that causes an immune reaction against cancer cells within the bladder. In April 2024, the U.S. Food and Drug Administration (FDA) approved the immunotherapy-boosting drug N-803 (Anktiva) in combination with BCG for the treatment of non-muscle invasive bladder cancer that is resistant to treatment with BCG alone.

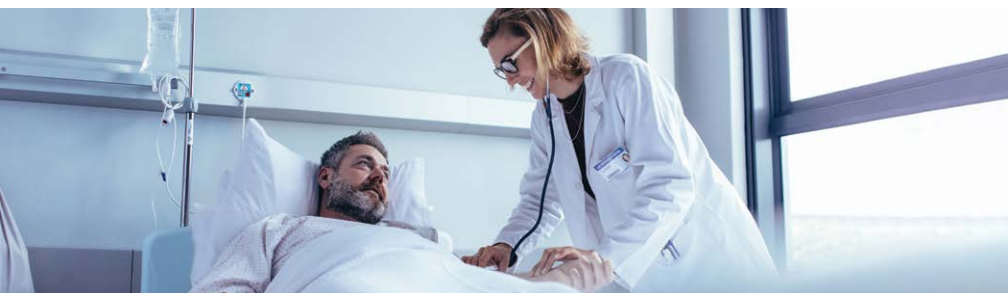
- **Chemotherapy.** Chemotherapy drugs are sometimes used as an intravesical treatment (directly inside the bladder); they include mitomycin C, thiotepa, doxorubicin, gemcitabine and valrubicin. Some multi-agent (more than one drug) chemotherapies are given sequentially such as gemcitabine and docetaxel (Gem/Doce).
- **Novel therapies.** For non-muscle invasive bladder cancers that do not respond to initial therapy, there have been recent FDA approvals for the immunotherapies pembrolizumab (Keytruda) and nivolumab (Opdivo), and the gene therapy nadofaragene firadenovec-vncg (Adstiladrin).

In cases where there is recurrent (returning) bladder cancer after treatment, a radical cystectomy is sometimes performed. In this surgical procedure, the entire bladder and surrounding lymph nodes are removed. This surgery also traditionally includes the removal of the prostate in men and the uterus, ovaries and part of the vagina in women.

Muscle-invasive bladder cancer

Surgery

If the cancer has invaded the muscle layer of the bladder wall or beyond, a radical cystectomy (as described in the previous section) is often performed. With the removal of the bladder, the surgeon will also create new ways for urine to be expelled from the body. Several options exist; the chosen option depends on the person's individual circumstances and their personal preferences.



Chemotherapy

Systemic (whole body) chemotherapy, often given before or after radical cystectomy, is designed to destroy cancer cells that may have spread beyond the bladder. Common drug combinations include MVAC (a mix of methotrexate, vinblastine, doxorubicin and cisplatin) and GC (gemcitabine plus cisplatin). Systemic chemotherapy is most often administered prior to surgery (neoadjuvant), but is sometimes given after surgery (adjuvant). When given prior to surgery, chemotherapy can destroy microscopic metastatic disease, increasing the chance that surgery will be successful.

Systemic chemotherapy can be the initial treatment for bladder cancer that is not treatable with surgery or is metastatic (has spread from the bladder to other organs).

Radiation Therapy

In certain situations, people with muscle-invasive bladder cancer are given the option of radiation therapy as an alternative to radical cystectomy. This treatment works better in smaller and less invasive tumors. Radiation therapy is most commonly given in combination with low-dose systemic chemotherapy. The chemotherapy makes the tumors more sensitive to the radiation treatment.

Targeted Therapy

Targeted therapy focuses on specific molecules and cell mechanisms thought to be important for cancer cell survival and growth, taking advantage of what researchers have learned in recent years about how cancer cells grow.

In January 2024 the FDA approved erdafitinib (Balversa) for the treatment of locally advanced or metastatic bladder cancer that has an FGFR3 genetic alteration and that has progressed after prior systemic therapy.

Immunotherapy

Many cancer cells carry “checkpoint” proteins that prevent the immune system from effectively attacking tumors. Certain immunotherapies, known as “checkpoint inhibitors,” allow the immune system to bypass these blocks.

There are four checkpoint inhibitors currently approved by the FDA for the treatment of people with urothelial carcinoma that is locally advanced or metastatic: atezolizumab (Tecentriq), nivolumab (Opdivo), pembrolizumab (Keytruda), and avelumab (Bavencio). These drugs can be used as an initial treatment, when the bladder cancer did not respond to chemotherapy, or to retain the benefits of prior therapy.

Antibody-drug conjugates

Antibody-drug conjugates work by combining a chemotherapy with an antibody that seeks out cancer cells.

- In December 2019 the FDA approved enfortumab vedotin-ejfv (Padcev) for the treatment of urothelial carcinoma that has progressed after chemotherapy and immunotherapy. In July 2021, the approval was expanded to include treatment of urothelial carcinoma that has progressed after at least one treatment regimen. In December 2023, enfortumab vedotin-ejfv was approved, in combination with the immunotherapy pembrolizumab, for the treatment of bladder cancer that has spread to other parts of the body or cannot be removed surgically.
- In April 2021 the FDA approved sacituzumab govitecan-hziy (Trodelvy) for the treatment of locally advanced or metastatic urothelial cancer that was previously treated with chemotherapy and immunotherapy.

The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and the quality of life of patients as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new valuable treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- Most clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit
- You can stop taking part in a clinical trial at any time for any reason.

Treatment Side Effects

All cancer treatments can cause side effects. It's important that side effects are reported right away so that your health care team can help manage them. It's important to remember that not all people being treated for bladder cancer experience all of these side effects, and people may experience side effects not listed here.

General side effects of bladder cancer treatment can include digestive tract symptoms (nausea, vomiting, diarrhea, loss of appetite) and fatigue. Your health care team can suggest ways to manage these side effects should they occur.

Side Effects of Chemotherapy

With intravesical chemotherapy (delivered directly into the bladder), the most common side effects are bladder irritation and painful urination. Since very little of the medicine is absorbed into the bloodstream, other more general side effects are uncommon.

The side effects of systemic chemotherapy depend on the type and dose of the therapy given and the length of time it is used, and can include:

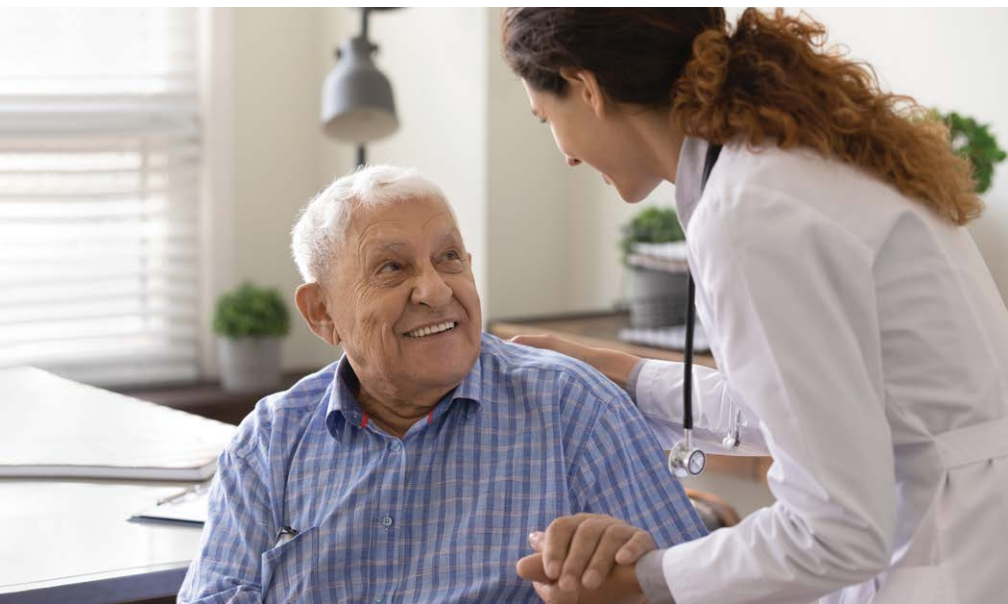
- Fatigue
- Nausea or vomiting
- Hair loss
- Changes in taste
- Increased risk of infection (from having too few white blood cells)
- Easy bruising or bleeding
- Peripheral neuropathy (numbness or tingling in hands and feet)

Side Effects of Immunotherapy

Immunotherapy drugs travel through the body, helping to enhance an immune response. Sometimes the immune system may attack healthy cells as well as cancer cells, and certain side effects may be experienced, including fatigue, decreased appetite, skin rash and digestive tract symptoms.

Side Effects of Radiation Therapy

Changes to the skin are the most common side effects of radiation therapy. Those changes can include dryness, swelling, peeling, redness and blistering. If a reaction occurs, you should contact a member of your health care team so the appropriate treatment can be prescribed. It's especially important to contact your health care team if there is any open skin or painful area, as this could be sign of an infection. Infections can be treated with an oral antibiotic or topical antibiotic cream. Radiation therapy can also lead to bladder irritation and diarrhea. Rarely, it can lead to incontinence and damage to the lining of the bladder.



General Side Effects

Some side effects may occur across treatment approaches; this section provides tips and guidance on how to manage these side effects should they occur.

Managing Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals that are chilled, which often makes food more easily tolerated.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.



Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade which provide electrolytes. Electrolytes are body salts that must stay in balance for cells to work properly.
- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary. If the diarrhea is bad enough that you need medicine, discuss it with your doctor or nurse.
- The BRAT diet (bananas, rice, applesauce, toast) and soluble fiber such as oats, bran and barley can help with diarrhea. Foods high in insoluble fiber, such as leafy greens and most fruits should be avoided as they can worsen diarrhea. Oily foods, caffeine and alcohol should also be avoided.
- Avoid food high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.

Managing loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow). Drink most of your liquids between meals.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna or trail mix.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.

Constipation

- As hydration is important, make sure to drink plenty of fluids. Also, limit your intake of caffeine as it can cause dehydration. Discuss with your doctor whether you can drink any alcohol as it can interact with your medications and may cause you to be dehydrated.
- Include foods high in fiber in your daily diet, such as fruit (especially pears and prunes), vegetables and cereals. If your health care team approves, you may want to add synthetic fiber to your diet, such as Metamucil, Citrucel or FiberCon.
- Be as physically active as you can, after checking with your doctor on the level of physical activity that is right for you.
- If your doctor has prescribed a “bowel regimen,” make sure to follow it exactly.





Managing Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. If you are taking a medication, your doctor may lower the dose of the drug, as long as it does not make the treatment less effective. If you are experiencing fatigue, talk to your doctor about whether taking a smaller dose is right for you.

There are a number of other tips for reducing fatigue:

- To be able to sleep well at night, avoid excessive sleep during the day.
- Take short walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.

Fatigue can be a symptom of other illnesses, such as anemia, diabetes, thyroid problems, heart disease, rheumatoid arthritis and depression. So be sure to ask your doctor if they think any of these conditions may be contributing to your fatigue.

Managing Pain

To help your doctor prescribe the best medication, it's useful to give an accurate report of your pain. Keep a journal that includes information on:

- Where the pain occurs
- When the pain occurs
- How long it lasts
- How strong it is on a scale of 1 to 10, with 1 being the least amount of pain and 10 the most intense
- What makes the pain feel better and what makes it feel more intense

There are a number of options for pain relief, including prescription and over-the-counter medications. It's important to talk to a member of your health care team before taking any over-the-counter medication to determine if they are safe and will not interfere with your treatments.

Physical therapy, acupuncture and massage may also be of help in managing your pain. Consult with a member of your health care team before beginning any of these activities.



Communicating With Your Health Care Team

As you manage your bladder cancer, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and get to know the members of your health care team, including doctors, nurses, nurse practitioners, physician assistants, dietitians, social workers and patient navigators.

Here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook (either on paper or in a digital format) will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, ask your most important questions first and be as specific as possible.

Bring someone with you to your appointments or have them be present during telehealth sessions. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. The person you bring may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice and instructions. You can also ask the person who accompanies you to take notes for you, either in your journal or on a tablet or smartphone.

Record your visit if your doctor allows it. Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

Incorporate other health care professionals into your team.

Your medical oncologist is an essential member of your health care team, but there are other health care professionals who can help you manage your diagnosis and treatment:

- Your primary care physician should be kept updated about your cancer treatment and any test results.
- Urologists specialize in the diagnosis and treatment of diseases of the urinary tract and are an important part of the multi-disciplinary team approach in the treatment of people with bladder cancer.
- Your local pharmacist is a great source of knowledge about the medications you are taking. Have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions.
- Make sure your oncologist knows of any other medical conditions you have or any pain you are experiencing so that they can consult with your primary care physician or specialist as needed.

Remember, there is no such thing as over-communication.

CancerCare's Free Support Services and Programs

It can be very difficult to receive a diagnosis of bladder cancer, and adjusting to the necessary changes in your life can be challenging.

CancerCare can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help in navigating the complicated health care system and offer information on support groups and other resources.

To learn more about how CancerCare helps, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

You will likely also build your own personal support network composed of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store, or ask a friend who's a good listener to come over for a chat.



MORE ABOUT BLADDER CANCER

Frequently Asked Questions

Q: Does it matter at what hospital or health care facility my treatment takes place?

A: There are many technical aspects involved in the treatment of bladder cancer, and it is best to be treated at a facility with a significant level of experience treating this type of cancer. Such facilities are highly familiar with potential complications, leading to overall better outcomes. Ask your health care team about the experience level of the facility at which your treatment will take place. If you are at all uncomfortable with the answers you are receiving, do not hesitate to seek a second opinion.

Q: What can I expect after treatment?

A: After treatment, you will be closely monitored by your health care team, who will check to make sure the cancer has not returned. The specifics of the monitoring depend on the treatment you were given and often include physical examinations, imaging tests, and routine blood and urine tests. If your bladder has not been removed, a cystoscopy (a minimally invasive procedure that allows your doctor to see the inside of your bladder) may also be performed.

For patients with a urinary “diversion” created after the removal of the bladder, follow-up care may include urine tests to check for infection, assessing and fixing any problems with urination control and checking for changes in kidney function through blood tests and imaging tests.

Q: What is a treatment summary and why is important?

A: Keeping your own records up-to-date in the form of a treatment summary can be helpful, as it allows you and your family members to have instant access to the specifics of your bladder cancer diagnosis and treatment. A treatment summary should include:

- Your name and date of birth
- Date of diagnosis
- Prescribed therapy/therapies, including dates started and stopped and dosages when appropriate
- Dates and types of baseline and post-diagnosis testing and the results of these tests
- Other medications and supplements you are taking
- Blood transfusion dates and results
- Names, affiliations and contact information of all members of your health care team

Ask the members of your health care team what they suggest be included. Take your personal record with you when you visit any doctor, not just your oncologist.

Q: What is squamous cell bladder cancer and how is it treated?

A: Squamous cell carcinoma (SCC) is a rare form of bladder cancer, representing less than five percent of all cases. Most commonly in response to chronic irritation, the epithelial lining of the bladder can gradually become squamous (scaly), potentially leading to the development of bladder cancer. The standard treatment for SCC is a radical cystectomy; however, additional treatment options are currently being researched.



Resources

CancerCare®

800-813-HOPE (800-813-4673)

www.cancercares.org

American Cancer Society

800-227-2345

www.cancer.org

Bladder Cancer Advocacy Network

888-901-BCAN (888-901-2226)

www.bcan.org

Medicine Assistance Tool

www.medicineassistancetool.org

CLINICAL TRIALS WEBSITES

ClinicalTrials.gov

www.clinicaltrials.gov

National Cancer Institute

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