

TREATMENT UPDATE:
Bladder Cancer

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Treatment Update: Bladder Cancer

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Each year, an estimated 81,000 adults in the United States are diagnosed with bladder cancer. Bladder cancer is nearly three times more common in men than in women. Among men, it is the fourth most common cancer. Bladder cancer is most commonly diagnosed at an early stage; if so, it can be highly treatable.

About 95 percent of bladder cancers are classified as transitional cell carcinomas (also called urothelial carcinomas) which arise from the cells that line the inside of the bladder. Urothelial cancers can also arise from other places along the urinary tract, including the ureters and urethra. In approximately 70 percent of transitional cell 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. There is a risk that once the bladder cancer has reached the muscle layer, it could spread to other parts of the body.

The most common early sign of bladder cancer is blood in the urine (hematuria). Other symptoms of bladder cancer may include frequent urination, painful urination, back pain and pelvic pain.

If bladder cancer is suspected, it is most often diagnosed via a cystoscopy, a minimally invasive procedure in which a narrow tube is inserted into the urethra (the passageway that allows urine to be excreted from the body), enabling the doctor to see the inside of the bladder. This procedure is sometimes combined with a biopsy, where a sample of cells is removed for further testing. Imaging tests, such as CT scans, PET scans and MRIs, may be used to determine if the cancer has spread outside of the bladder.

Treatment Options

The course of treatment for bladder cancer is often determined after consultations with a urologist (doctor who specializes in treating the urinary system), 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 (TUR).** A small electrified wire loop is passed through a cystoscope into the bladder and is used to biopsy and 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) immune therapy that causes an immune reaction against cancer cells within the bladder.
- **Chemotherapy.** Chemotherapy drugs are sometimes used as an intravesical treatment. These drugs include mitomycin C, thiotepa, doxorubicin, gemcitabine and valrubicin.

Advanced bladder cancer

Surgery

If the cancer has invaded the muscle layer of the bladder wall or beyond, a surgical procedure called a radical cystectomy is often performed, in which the entire bladder and surrounding lymph nodes are removed. This surgery also includes the removal of the prostate in men and certain reproductive organs in women.

With the removal of the bladder, the surgeon will also create new ways for the person to expel urine. Several options exist; the best option depends on individual circumstances and preferences. It's important for people to have an in-depth conversation with their surgeon about the advantages and disadvantages of each option.

Chemotherapy

Systemic (whole body) chemotherapy, often used in conjunction with a radical cystectomy, is designed to destroy cancer cells that may have spread beyond the bladder. Systemic chemotherapy is most often administered intravenously (through a vein). 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 (called "neoadjuvant"), but is sometimes given after surgery. Chemotherapy is also given as the primary

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

Radiation Therapy

Certain people with muscle-invasive bladder cancer are sometimes given the option of radiation therapy as an alternative to radical cystectomy. Radiation therapy is most commonly given in combination with chemotherapy.

Immunotherapy

Immunotherapy is a treatment that uses the immune system to fight illnesses, including cancer. Many cancer cells carry “check-point” proteins that prevent the immune system from effectively attacking tumors, but certain immunotherapy drugs, known as “checkpoint inhibitors,” are able to bypass these blocks.

Since 2016, the U.S. Food and Drug Administration (FDA) has approved five immunotherapy drugs, all checkpoint inhibitors, for the treatment of people with urothelial carcinoma that is locally advanced or metastatic.

Atezolizumab (Tecentriq), nivolumab (Opdivo), pembrolizumab (Keytruda), durvalumab (Imfinzi) and avelumab (Bavencio) work by targeting the proteins PD-1 and/or PD-L1 that can prevent the body’s immune system from attacking tumors.

Atezolizumab, nivolumab, pembrolizumab, durvalumab and avelumab are approved for the treatment of individuals whose cancer has progressed after treatment with platinum-containing chemotherapy. Atezolizumab and pembrolizumab are also approved as a first-line treatment for patients with advanced or metastatic bladder cancer who are unable to be treated with cisplatin-containing chemotherapy.

Pembrolizumab is also approved to treat people with inoperable metastatic tumors that have specific genetic features, such as microsatellite instability (MSI) or mismatch repair deficiency (dMMR), which can prevent DNA within cells from repairing itself.

Utilizing immunotherapy in combination with chemotherapy is currently being studied in clinical trials as a treatment approach for bladder cancer.



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 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 you report any side effects that you experience to your health care team so they can help you manage them. Report them right away—don't wait for your next appointment. Doing so will improve your quality of life and allow you to stick with your treatment plan. It's important to remember that not all people experience all side effects, and people may experience side effects not listed here.

Side Effects of Chemotherapy

With intravesical chemotherapy, the most common side effects are bladder irritation and painful urination, but side effects affecting the whole body are uncommon since very little of the drug is absorbed into the bloodstream.

The side effects of systemic chemotherapy depend on the type and dose of drugs given and the length of time they are used, and can include:

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

Side Effects of Immunotherapy

Immunotherapy travels through the bloodstream, helping to prompt 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 and digestive tract symptoms. The management of these potential side effects is discussed later in this booklet.

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, contact 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 areas, as this could indicate 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

There are certain side effects that may occur across different treatment approaches. Following are tips and guidance for managing these side effects.

Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals cold or at room temperature, 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 that provide electrolytes as well as liquid. 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.
- Choose foods that contain soluble fiber, such as beans, oat cereals, oranges and flaxseeds. High-pectin foods like peaches, apples, oranges, grapefruit, bananas and apricots can also help to avoid diarrhea.
- Low fat food choices are less likely to cause diarrhea than fatty, greasy or fried foods. The fats you eat should come from healthy sources, such as olive oil, canola oil, avocado, olives, nuts and seeds.

Loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories and to 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.

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:

- Take several short naps or breaks.
- 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.

There are also prescription medications that may help. Your health care team can provide guidance on whether medication is the right approach for your individual circumstances.

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 he or she thinks 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 in order to determine if they are safe and will not interfere with your treatments. Many pain medications can lead to constipation, which may make your pain worse. Your doctor can prescribe medications that help to avoid constipation.

Physical therapy, acupuncture and massage may also be of help in managing your pain. Other techniques, such as mindfulness meditation, deep breathing exercises and yoga may also be helpful. 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 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 the members of your health care team, including nurses, 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 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. Keep a diary of your daily experiences with cancer and treatment. You can separate your journal or notebook into different sections to help keep it organized.

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

Bring someone with you to your appointments. 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 who accompanies you can serve as a second set of ears. He or she 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. If you cannot write down the answers, ask the person who accompanies you to do that for you. If you have a mobile device, like a tablet or smartphone, ask if you can use it to take notes. Writing notes will help you review the information later.

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 bladder 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 patients 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 your 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 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 provide 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, comprised 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; 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: As there are many technical aspects involved in the treatment of bladder cancer, it is best to be treated at an institution with a lot of experience caring for patients with that specific type of cancer. One reason is that such institutions 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: Are there any targeted therapies approved for the treatment of bladder cancer?

A: In recent years, researchers have learned more about the genetics of bladder cancer and the molecular changes that occur in its tumors. This has led to ongoing clinical trials of targeted therapies, which are therapies designed to target the specific cell mechanisms that are important for the growth and survival of cancer cells. Although the early study results are promising, there are currently no targeted therapies approved for treatment of bladder cancer.

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 5 percent of all cases. 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.

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, routine blood and urine tests and imaging 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.



Resources

CancerCare®

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

www.cancercares.org

American Cancer Society

800-227-2345

www.cancer.org

Cancer.Net

Patient information from the American Society of Clinical Oncology

888-651-3038

www.cancer.net

Bladder Cancer Advocacy Network

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

www.bcan.org

Partnership for Prescription Assistance

888-477-2669

www.pparx.org

CLINICAL TRIALS WEBSITES

EmergingMed

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