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. 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. Transitional cell 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 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 expelled 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 (a 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 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) treatment that causes an immune reaction against cancer cells within the bladder.
- **Chemotherapy.** Chemotherapy drugs are sometimes used as an intravesical treatment; they 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 the uterus, ovaries and part of the vagina in women.

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 best option depends on the person's individual circumstances and their personal 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 (neoadjuvant), but is sometimes given after surgery (adjuvant).

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

In certain situations, 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 "checkpoint" proteins that prevent the immune system from effectively attacking tumors. Certain immunotherapies, 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 patients 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. These five treatments are approved for the treatment of bladder cancer that has progressed after being treated with chemotherapy that contains cisplatin.

Atezolizumab and pembrolizumab are also approved as a first-line treatment for people with advanced or metastatic bladder cancer who are unable to be treated with cisplatin-containing or carboplatin-containing chemotherapy.

Pembrolizumab is also approved to treat patients 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.

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 April 2019, the FDA approved erdafitinib (Balversa) for the treatment of locally advanced or metastatic bladder cancer that has an FGFR3 or FGFR2 genetic alteration and that has progressed after treatment with chemotherapy that contains cisplatin.

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 patients experience all side effects, and patients 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. As 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
- 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, skin rash 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 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 areas, 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.

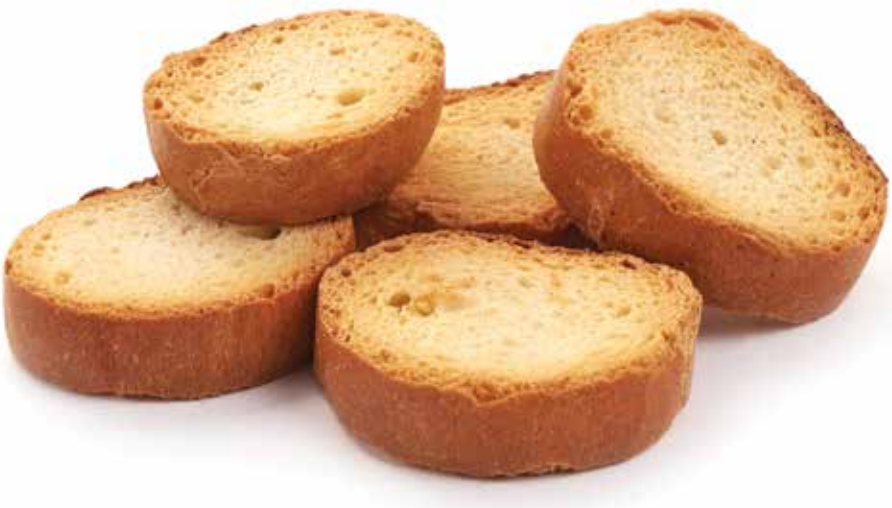
General Side Effects

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 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. 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 medications are available for diarrhea, but should be used only if necessary. If the diarrhea is bad enough that you need medicine, contact a member of your health care team.
- Choose foods that contain soluble fiber, like beans, oat cereals and flaxseed, and high-pectin foods such as peaches, apples, oranges, bananas and apricots.
- Avoid foods high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.

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.

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 during the day.
- Take 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, such as modafinil. Your health care team can provide guidance on whether medication is the right approach for your individual circumstances.

Managing Pain

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 it is safe and to make sure it will not interfere with your treatment. 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. 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 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. 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.

Cancer*Care*'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.

Cancer*Care* 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 Cancer*Care* 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.

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: A treatment summary, sometimes called a "shadow chart," is a document that you create and keep in your possession. Maintaining your own records 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 post-diagnosis testing, and the results of these tests
- Other medications and supplements you are taking
- Names, affiliations and contact information of all members of your health care team

Talk to your doctor or a member of your health care team about your intention to create a treatment summary, and ask what else they suggest be included. Take your treatment summary with you when you visit any doctor, not just your oncologist or urologist.

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. 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.

Notes

Resources

CancerCare®
800-813-HOPE (800-813-4673)
www.cancercare.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

Medicine Assistance Tool
www.medicineassistancetool.org

CLINICAL TRIALS WEBSITES

EmergingMed
www.emergingmed.com

National Cancer Institute
www.cancer.gov

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