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#Reference From NCCN Guidelines

Advanced-Stage Prostate Cancer

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The prostate is a gland located deep inside the pelvis. Everyone with a prostate has a chance of getting prostate cancer. This chapter offers an overview of this common cancer.

What is prostate cancer?

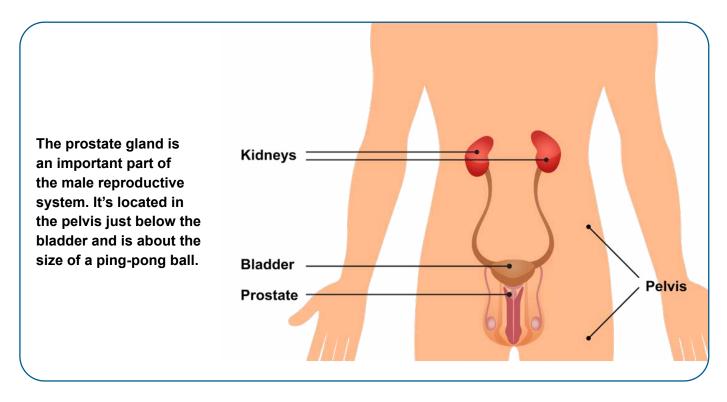
Prostate cancer is a disease where cells in the prostate gland grow out of control.

The prostate is a small gland located just below the bladder in the pelvis, deep inside the area of your body between your hip bones. The prostate is about the size of a ping-pong ball and is an important part of the male reproductive system. Besides the prostate, the male reproductive system includes the penis, seminal vesicles, and testicles.

Cancer is what happens when something goes wrong with the natural cell process causing some cells to grow out of control.

Cancer cells don't behave like normal cells. Cancer cells develop genetic changes (mutations) that allow them to multiply and make many more cancer cells. The cancer cells crowd out and overpower normal cells. This can end up harming the body.

Cancer cells survive much longer than normal cells do. They can replace many normal cells and cause organs to stop working well. Cancer cells can also spread outside the prostate to other areas of the body.



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What are the symptoms of prostate cancer?

A symptom is a feeling or problem that can indicate a disease or condition. Prostate cancer often grows slowly and shows no symptoms for a long time. You don't have to have symptoms to have prostate cancer.

Symptoms, if they occur, may include:

- Blood in the urine or semen
- > Burning or pain while urinating
- Unexplained weight loss
- Bone, hip, or back pain

It's important to know that prostate cancer has many of the same symptoms as a condition called enlarged prostate (also called benign prostatic hyperplasia, or BPH). BPH is much more common than prostate cancer. It's difficult to tell the difference between the two conditions based on symptoms alone. Be sure to tell your health care providers if you have any of these symptoms, because you may need special testing:

- > Urinating frequently, especially at night
- > Weak or intermittent urine stream
- > Trouble urinating or straining to urinate
- Trouble holding in urine
- Feeling like your bladder hasn't fully emptied
- > Dull pain in your groin or pelvis
- Erectile dysfunction (difficulty getting an erection) or painful ejaculation

What causes prostate cancer?

Many people who develop cancer wonder where it came from and how they got it. Doctors don't know exactly what causes prostate cells to grow out of control (become cancerous). But several factors are linked to a higher risk of prostate cancer. These are called risk factors. A risk factor is anything that increases your chance of getting cancer.

Risk factors don't necessarily cause prostate cancer, but people with prostate cancer usually have one or more of these risk factors:

Age

The biggest risk factor for prostate cancer is age. Prostate cancer is diagnosed most often in those aged 65 years and above. Your chances of getting prostate cancer increase as you become older.

Family history

Your family health history is information about the diseases and health conditions in your family. A family history reflects a pattern of certain diseases among family members. Having a close family member with prostate cancer (a sibling or parent) increases the chance of getting it yourself. Those with a family history of certain other cancers (breast, ovarian, colon, pancreatic, and other cancers) may also be at a higher risk for prostate cancer.

Genetic factors

When cancer "runs in the family," genetic testing can be done to find specific genetic

Where does the prostate fit in?

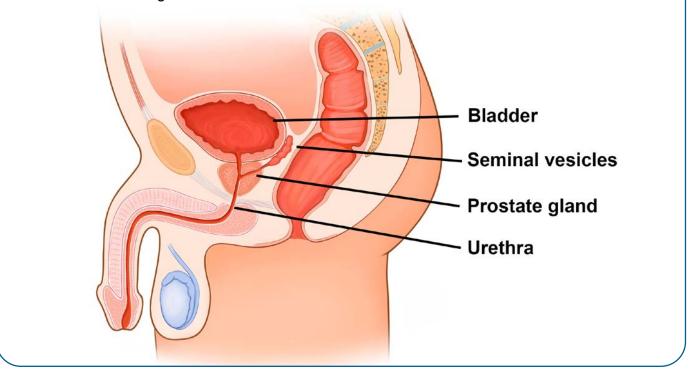
The prostate is a small gland located in the pelvis—the area between your hips. The prostate is important for sexual reproduction.

Prostate: A gland in the male reproductive system. A gland is an organ that makes fluids or chemicals the body needs. The prostate gland makes a fluid that nourishes and helps transmit sperm. The prostate also contains muscles that help propel semen through the urethra during ejaculation.

Semen: A fluid made up of liquids from the prostate and the seminal vesicles as well as sperm from the testicles. During ejaculation, semen is released from the body through the urethra and out through the penis.

Urethra: A tube that carries urine from the bladder and out of the body. The prostate surrounds the urethra just beneath the bladder.

Seminal vesicles: Two glands that make and store another part of the fluid that becomes semen. The seminal vesicles are located above the prostate and behind the bladder.



Bladder: An organ that holds urine.

NCCN Guidelines for Patients® Advanced-Stage Prostate Cancer, 2023 changes (mutations) known to be linked with prostate cancer and other cancers. For instance, having an inherited genetic mutation in the *BRCA2* gene increases the risk of getting prostate cancer. But genetic abnormalities that aren't inherited can occur, too.

Race

In the United States, Black people are more likely than White people to develop prostate cancer. Prostate cancer in Black people is also more likely to occur at an earlier age and be more aggressive and more advanced when diagnosed. Black people are also twice as likely to die from prostate cancer compared with White people. These differences are due to barriers to accessing health care (including early detection screening), as well as biological and genetic factors, and other causes. Specialists are researching each of these areas.

Diet and lifestyle

Eating food that's high in fat, such as meat and dairy products, has been linked with an increased risk of prostate cancer. Eating more fruits and vegetables may reduce this risk. Exercise may also decrease the likelihood of dying from prostate cancer. On the other hand, smoking and obesity increase the risks of developing prostate cancer and dying from it.

These risk factors aside, anyone with a prostate has a risk of getting prostate cancer. Prostate cancer is the second-most common cancer in American males after skin cancer.

What does aggressive mean?

When health care professionals describe cancer as aggressive, they mean the cancer is likely to grow or spread more rapidly than average.

Aggressive is also used to describe therapy that's stronger or more intense than other treatment options.

What is advanced-stage prostate cancer?

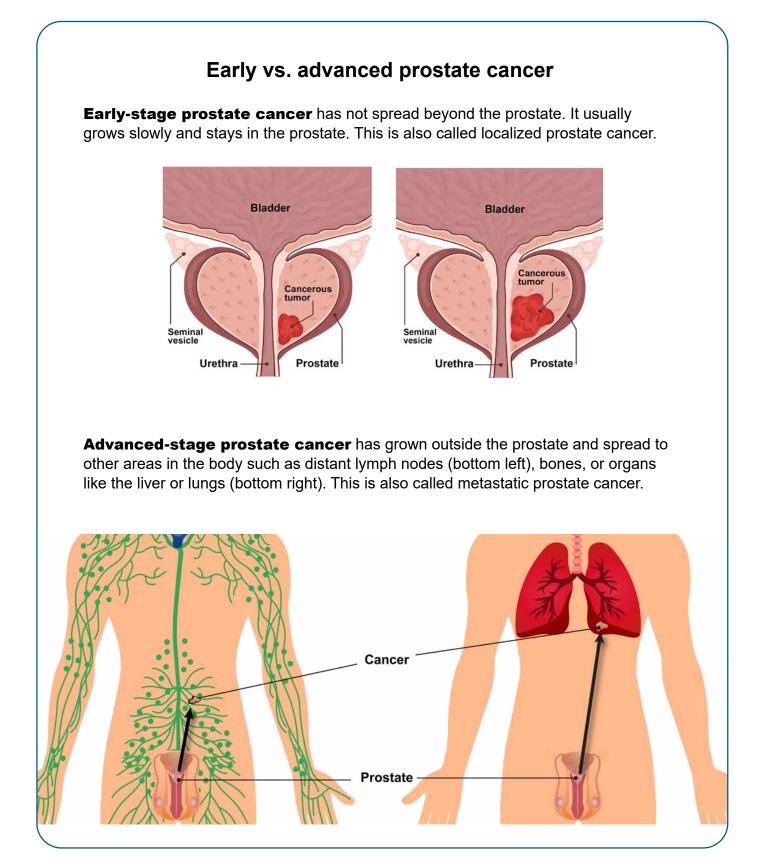
Prostate cancer can be grouped into earlystage cancer or advanced-stage cancer.

Early stage

Early-stage prostate cancer has not spread beyond the prostate. The cancer usually grows slowly and stays in the prostate. Cancer that is contained entirely within the prostate is called localized prostate cancer.

More information about early-stage prostate cancer can be found at <u>NCCN.org/</u> <u>patientguidelines</u> and on the <u>NCCN Patient Guides for</u> <u>Cancer</u> app.





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Advanced stage

Advanced stage means that the cancer has spread beyond the prostate to other areas in the body. This spreading is called metastasis or metastatic cancer. Metastatic prostate cancer may spread to the lymph nodes, bones, liver, lungs, and other organs.

This book is all about advanced-stage prostate cancer.

- Cancer that grows from the prostate gland to nearby areas such as lymph nodes, but no farther, is called regional prostate cancer.
- Cancer that spreads beyond the prostate to other parts of the body is called distant metastatic prostate cancer or simply metastatic prostate cancer.

How does prostate cancer spread? Cancer cells use the bloodstream like a highway to travel to distant areas in the body. Cancer cells can also spread through the lymphatic system. The lymphatic system is a network of organs and vessels that fights infections and circulates a clear fluid called lymph throughout the body. A normal and important part of this system are the lymph nodes. Lymph nodes are small, disease-fighting clusters that filter the lymph fluid to remove germs. Lymph vessels and nodes are found everywhere in the body.

Some patients have advanced-stage prostate cancer when they're first diagnosed. Others develop advanced-stage cancer after having treatment for early-stage cancer.

Can prostate cancer be cured?

Advanced-stage prostate cancer is usually a life-long disease. But treatment can slow down its growth, reduce symptoms, and prolong your life. Treatments for advanced prostate cancer include hormone therapy, chemotherapy, immunotherapy, targeted therapy, radiation therapy, radiopharmaceuticals, and other therapies.

It's true that prostate cancer in the advanced stage can be fatal for some patients. But in the past few years, improved detection methods and better treatments have been reducing the number of deaths from prostate cancer in patients of all races and ethnicities. Many people with advanced-stage prostate cancer continue to live with the cancer and, in the end, some may die from something else.

Scientists have learned a great deal about prostate cancer in recent years. As a result, today's detection methods and treatments work better than those in the past. Also, many patients with prostate cancer have more treatment choices now than they had before.

What's the best treatment?

The best treatment for prostate cancer is the treatment that's right for you. Importantly, your health care team should follow best practices. This book is based on the best practices for treating advanced prostate cancer. Best practices come from the latest research and methods at top cancer centers. Your treatment team should personalize your care following the best practices.

Key points

- Prostate cancer develops when cells in the prostate gland grow out of control.
- Not everyone with prostate cancer has symptoms.
- Age is the biggest risk factor for prostate cancer. As you age, your chances of developing prostate cancer increase.
- Most prostate cancers are diagnosed in people over the age of 65.
- Having a close family member with prostate cancer means that you have a higher chance of getting it yourself.
- Everyone with a prostate is at risk for prostate cancer. Black people are at greater risk.
- Early-stage prostate cancer hasn't spread outside the prostate.
- Advanced-stage prostate cancer has spread outside the prostate to other areas in the body. This spreading is called metastasis.
- Cancer cells use the bloodstream and lymphatic system to spread to other areas of the body.
- Advanced-stage prostate cancer is usually a life-long disease. Treatment can slow it down, reduce its symptoms, and help people live longer.
- Better detection and treatments for prostate cancer have reduced the number of deaths in people of all races and ethnicities.

Many new tests and treatments are now available for advanced prostate cancer. Seek care or a second opinion from a medical center that specializes in prostate cancer.

2 Tests for advanced prostate cancer

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If you haven't yet been diagnosed, testing is necessary to find out if you have prostate cancer and whether it has spread. Testing also helps your care team plan the best treatment.

Health care providers use a variety of tests to find prostate cancer and to determine how advanced the cancer is. Tests are used to plan treatment, check how well treatment is working, and monitor your health after treatment ends. This chapter will help you know what tests you may have and what to expect during testing. When you go for testing, bring someone with you to listen, ask questions, and write down the answers.

Not every person with prostate cancer will receive every test listed here.

Common prostate tests

Common prostate cancer tests are the prostatespecific antigen (PSA) test, PSA doubling time, and digital rectal exam. These tests are used to detect the possibility of prostate cancer in someone who's undiagnosed. They're also used to check and monitor prostate cancer in patients who have been diagnosed.

PSA test

This test measures the amount of PSA in your bloodstream. PSA is a protein made inside the prostate gland. Its job is to help semen transport sperm. If there's something wrong with the prostate like prostate cancer—the prostate may make more PSA. An unusually high amount of PSA in the blood may be a sign of prostate cancer. Likewise, an increase in PSA after treatment may indicate that the treatment is losing effectiveness. However, high PSA levels can vary by age and other factors.

PSA level is measured in nanograms of PSA per milliliter (ng/mL) of blood.

PSA doubling time

PSA doubling time is a test that measures how long it takes for your PSA level to double. It can be used to detect how active or aggressive the cancer may be. If your PSA level doubles in a short period of time (6 months or less, for example), it suggests that the cancer is growing rapidly. If it takes longer to double (10 months or more), the cancer is growing slowly and may not need a new treatment right away.

Digital rectal exam

A digital rectal exam (also called a prostate exam) is the simplest and most direct way to check the size and texture of your prostate. For this test, the doctor will insert a gloved finger into your rectum to feel your prostate. An irregular or hardened part of the prostate could be a sign of a tumor.

Not all parts of the prostate can be felt during this exam, though. So the digital rectal exam is usually paired with a PSA test and other factors—your age, race, family history, and more—to determine whether you need further testing.

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General health tests

Health history and physical exam

Your care team needs to have all your health information. They'll ask you about any health problems and treatments you've had in your life. Be prepared to talk about any illness or injury you've had and when it happened. Also tell your doctor about any symptoms you have.

Bring a list of old and new medicines and any over-the-counter medicines, herbs, or supplements you take. Some of these (such as saw palmetto or St. John's wort) can cause changes in your PSA level, so your doctor needs to know if you're taking them.

A physical exam is a check of your body for any signs of disease. Your health care provider may feel for enlarged glands (lymph nodes) in your groin, underarms, and neck.

Family history

Some cancers and other diseases can run in families. Your doctor will ask about the health

history of family members who are blood relatives. This information is called a family history.

It's important to ask members from both sides of the family about all cancers, not just prostate cancer. Ask family members about other health issues like heart disease and diabetes, at what age they were diagnosed, and if anyone died from cancer. Share this information and any changes to your family history with your care team.

Symptoms and quality of life

Your doctor or another member of your care team will ask you a series of questions about what symptoms you may have (such as peeing frequently, difficulty peeing or pooping, or sexual problems). You'll also be asked how these symptoms affect your quality of life. Quality of life refers to your overall satisfaction with your well-being and your ability to participate in regular activities. It's important to answer all these questions honestly and completely so your care team has full and upto-date information about how you're doing.

Taking supplements?

It's important to bring a list of old and new medicines to your doctor's office when you begin testing. It's also important to tell your treatment team if you're using any complementary medicines, especially supplements, vitamins, or herbs. Some of these can interfere with your cancer tests or treatment. This may reduce the effectiveness of treatment or cause more side effects.



Life expectancy

Life expectancy is the average lifespan of a person. It's measured in years. An estimate of your life expectancy may be a key factor in deciding which tests and treatments you'll need. For example, some people with other health risks or conditions may be advised to wait until symptoms appear before having tests or starting treatment for prostate cancer. There may be no benefit to having additional tests or undergoing treatment if you don't have symptoms or if you have other more lifethreatening health conditions.

It's important to know that life expectancy when used for cancer care—is an estimate based on large numbers of people with similar age and features of cancer. That means life expectancy can be applied to a certain population or age range, but it's not as easy to make a precise estimate of the lifespan of an individual person.

Diagnosis vs. prognosis

What's the difference between your diagnosis and your prognosis? These two words sound alike but they're very different.

Diagnosis is identifying an illness based on tests. Your diagnosis names what illness you have.

Prognosis is the likely course and outcome of a disease based on tests and your response to treatment. Your prognosis predicts how your illness will turn out.

Diagnostic tests

Diagnostic tests are used to confirm you have cancer. They're also used to find out if the cancer is localized or advanced. Diagnostic tests can help plan treatment after you've been diagnosed and can detect whether the cancer is still growing or spreading after treatment.

Imaging tests

An imaging test takes pictures (images) of the insides of your body. The images can reveal cancer, including its size, location, and other features such as the size of the prostate itself. The images may show where the cancer started (primary tumor) and whether the cancer has spread (metastasized).

Imaging can come before, during, or after a biopsy. Imaging may also be used after cancer treatment to see how well it worked and to check if the cancer comes back.

Imaging methods for prostate cancer include ultrasound, bone scan, CT, MRI, PET, or a combination of these.

CT scan

A computed tomography (CT or CAT) scan uses x-rays and computer technology to take pictures of the inside of the body. CT takes many x-rays of the same body part from different angles. The computer combines all the x-ray pictures to make a single detailed image. A CT scan of your abdomen and/or pelvis may be used to look for cancer that has spread beyond the prostate. CT scans are good at seeing enlarged lymph nodes and the area around the prostate, and they can indicate if the cancer has spread to the lungs, liver, or other organs. A CT scan can also measure the size of a tumor.

For the scan, you'll be alone but a technician will operate the machine in a nearby room. The technician will be able to see, hear, and speak with you at all times. A CT scan is done in about 30 seconds, but the entire process takes 20 to 30 minutes.

MRI scan

A magnetic resonance imaging (MRI) scan uses radio waves and powerful magnets to take pictures of the inside of the body. An MRI can be used to get a more detailed view of the cancer within the prostate. It's also used to see if cancer has spread to nearby lymph nodes or to the bones in your pelvis. MRI scans can also help to plan treatment, and may be used after treatment to check whether the cancer has come back (recurrence).

An appointment for an MRI scan can take about 1 to 2 hours, including 30 to 60 minutes of actual scanning time. You'll need to remain as motionless as possible during each scan. You may be positioned with pillows or bolsters to help you keep still.

Because an MRI uses magnets, don't bring any metal objects (jewelry, cell phone, wristwatch, belts with metal buckles) into the imaging room.

PET scan

A positron emission tomography (PET) scan highlights cells in your body that may be cancerous. A PET scan is used after you've been diagnosed to determine the extent of your cancer or to see if it has metastasized. PET imaging can also show how well treatment is working.

PET imaging

A positron emission tomography (PET) scan highlights cells in your body that may be cancerous. A PET scan is used after you've been diagnosed to determine the extent of your cancer or to see if it has metastasized. PET imaging can also show how well treatment is working.



A PET scan requires injecting a radioactive substance called a tracer into your bloodstream. It takes about an hour for the tracer to circulate throughout your body. The tracer targets your cancer cells, which show up as bright spots on the scan. Afterward, the radiotracer is passed out of your body in your urine.

A PET scan appointment can take 1 to 2 hours, including about 30 minutes of actual scanning time.

Because PET uses a different imaging method, it's often combined with other types of imaging, such as CT or MRI, to provide an even more detailed image. This combined method is called a PET/CT or PET/MRI scan.

PSMA-PET

PET scans use different types of tracers. The most common tracer in prostate cancer locates a protein called prostate-specific membrane antigen (PSMA) on the surface of prostate cancer cells. Prostate cancer cells make a lot of PSMA, so doctors developed tracers that target this specific protein.

PSMA-PET imaging is especially useful for detecting cancer that has spread to nearby lymph nodes or has metastasized to farther areas. It's also used to monitor prostate cancer for recurrence.

Bone scan

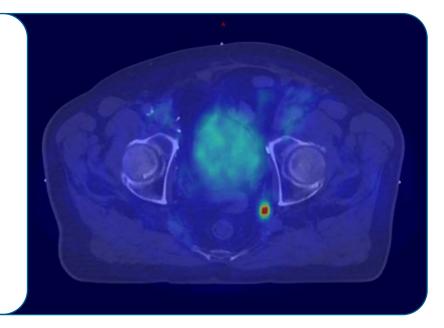
A bone scan can detect whether cancer has spread to your bones. A bone scan may be used if you have bone pain, have a high risk for bone metastasis, or have changes in certain test results. Bone scans may also be used to monitor treatment.

A bone scan uses a radioactive tracer to make pictures of the inside of bones. Before the pictures are taken, the tracer is injected into your bloodstream. It can take a few hours for the tracer to enter your bones.

A special camera will take pictures of the tracer in your bones. Areas of bone damage

PET/CT scan of prostate cancer

This image combines PET and CT scans to show a cross-section of a patient's pelvis. The greenish circle identifies cancer in the prostate, while the intense red dot indicates cancer that has spread to a lymph node in the pelvis.



NCCN Guidelines for Patients[®] Advanced-Stage Prostate Cancer, 2023 absorb more tracer than healthy bone. These areas show up as bright spots in the scans.

Biopsy

A biopsy is a procedure in which a sample of cells, fluid, or tissue is removed from your body and tested for cancer. A biopsy may be taken from the prostate, the metastasis (an area of cancer that has spread outside of the prostate), or sometimes both.

Biopsy of the prostate

A prostate biopsy is usually performed by a urologist. A urologist is a doctor who's an expert in treating diseases of the urinary system and the male reproductive organs.

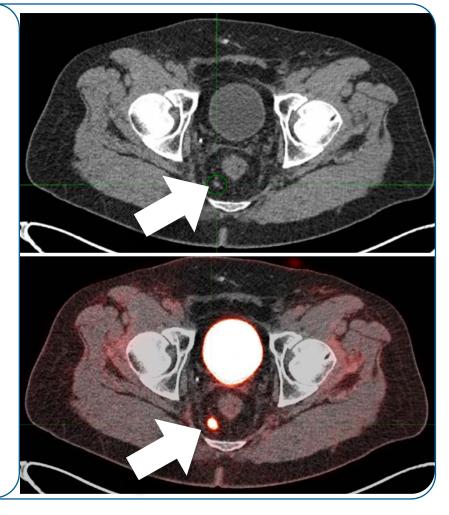
For this procedure, the urologist will insert a hollow needle into the prostate gland using a video display to guide it. The video images come from an ultrasound, MRI, or CT scan, or a combination of these technologies. The needle is inserted either through the rectum or through the perineum (the skin between the anus and scrotum).

PSMA-PET scan of prostate cancer

A CT scan for a patient treated for prostate cancer shows a crosssection of the body at the pelvis. The CT pinpoints a lymph node that appears normal (top image).

But a PMSA-PET scan of the same lymph node highlights prostate cancer cells (arrow in bottom image).

Images: University of Chicago Medicine



When the urologist removes the needle, it will pull out a small sample of prostate tissue called a core. Your urologist will take 12 or more core samples from different parts of the prostate. Checking different areas provides a more complete evaluation of cancer throughout the gland.

After the biopsy samples are removed, a pathologist will examine the samples under a microscope and test them for cancer cells. The pathologist will find out how many of the core samples contain cancer and will also measure the percentage of cancer in each core. With this information, the pathologist can estimate the amount of cancer in the prostate and how aggressive it may be. Also, by knowing where each core sample was taken, the pathologist can figure out whether the cancer is concentrated in a certain section of the prostate. The pathologist will put these results into a report. Ask your doctor to review the pathology report with you.

Biopsy of the metastasis

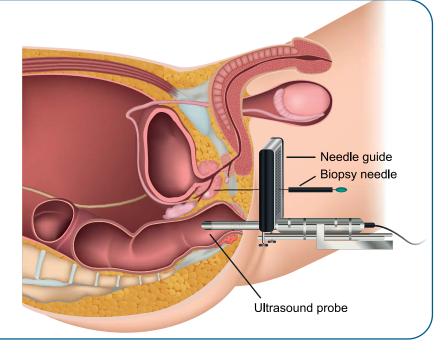
A biopsy of a metastasis can be taken from a lymph node, an internal organ, or a bone. This biopsy is performed in a similar way to a prostate biopsy—using a hollow needle to remove cores of tissue. However, this procedure may be more complicated than a prostate biopsy. For example, a bone biopsy is a more difficult procedure because it's harder to bore into bone.

Sometimes, a blood sample is taken, also called a "liquid biopsy," to look for cancer cells in the blood.

By the way, having a biopsy can't make your cancer worse. Medical research has shown there's no increased risk of prostate cancer spreading or worsening due to a biopsy.

Biopsy of the prostate

A biopsy removes a sample of tissue that is tested for cancer. This is a transperineal biopsy, in which a needle is inserted through the perineum and into the prostate. An ultrasound probe, which goes into the rectum, helps the doctor guide the needle into the prostate. MRI scans of your prostate may be combined with the ultrasound image to provide a highly accurate picture of the cancer.



Genetic tests

A genetic test is used to find abnormal changes in your genes. Genes are small segments of DNA inside every cell. Genes provide the instructions to tell the cell how to make proteins, which carry out a lot of important functions in the body.

Once in a while, a gene will have or develop an abnormal change (also called a mutation). A mutation is when something is different in your genes than in most other people's genes. Sometimes an abnormal change can cause a gene to make the wrong type of protein or make no protein at all. This abnormality can affect the cell, which may in turn cause a disease—such as cancer.

Mutations can be passed down in families, in which case they occur in every cell in your body. Or mutations can occur spontaneously in just some of your cells. In other words, they may be present before you're born (called an inherited or germline mutation) or occur on their own later in life (called an acquired or somatic mutation). Either genetic abnormality can be used as a biomarker. A biomarker is something found in your body that can be measured to assess your health. A biomarker could also point to a specific therapy.

Genetic tests for prostate cancer look for germline or somatic mutations:

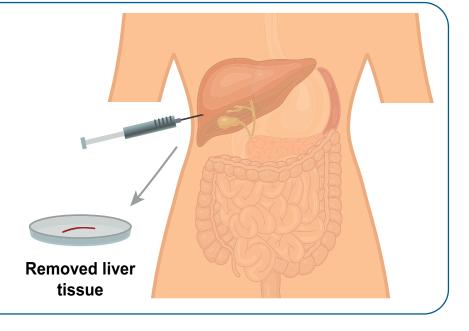
Germline testing

Sometimes, mutations in genes inherited from your parents can increase the risk of different cancers. Other family members might also carry these mutations. If you have a family history of cancer, your doctor might suggest genetic germline testing to find out if you have an inherited cancer risk.

The goal of this type of genetic testing is to look for germline (inherited) mutations that occur in every cell in your body. Genetic

Biopsy of the metastasis

Prostate cancer may metastasize to lymph nodes, bones, or internal organs. A biopsy of a metastasis (as seen here, taken from the liver) uses a hollow needle to remove a small core of tissue. The tissue is tested in a lab to look for cancer cells.



NCCN Guidelines for Patients® Advanced-Stage Prostate Cancer, 2023 germline testing is done using a sample of your blood, urine, or saliva.

For prostate cancer, germline testing looks for characteristic changes in these genes: *BRCA1, BRCA2, ATM, CHEK2, MLH1, MSH2, MSH6, PALB2, PMS2,* and others. Some mutations can put you at risk for more than one type of cancer. Germline mutations in genes like *BRCA1 or BRCA2* are also related to breast, ovarian, and pancreatic cancer. Germline mutations in *MSH2, MSH6, MLH1,* and *PMS2* are related to colorectal and uterine cancers in addition to prostate cancer.

If a germline mutation is suspected based on your family's or your own health history, you should ask about genetic testing. Your doctor can talk to you about testing or refer you to a genetic counselor. A genetic counselor is an expert who has special training in genetic diseases. A genetic counselor can help you decide whether you would like to undergo germline testing and also help you interpret the results of these tests.

Germline testing is recommended if you have prostate cancer and any of the following:

- Family members or relatives who have or had prostate cancer, breast cancer, ovarian cancer, intestinal cancer, and certain other cancers
- Family history of mutations in certain genes including BRCA1, BRCA2, ATM, CHEK2, and others
- High-risk, regional, or metastatic prostate cancer regardless of family history
- Ashkenazi Jewish ancestry
- Current or previous breast cancer

NCCN Guidelines for Patients[®] Advanced-Stage Prostate Cancer, 2023 Talk to your medical providers and/or a genetic counselor about your family history of cancer.

Somatic (tumor) testing

A molecule that's released by a tumor can be used as a biomarker for cancer. So this type of testing looks at the molecular components of a tumor for these cancer biomarkers.

Somatic testing (also called molecular tumor testing or tumor profiling) requires a biopsy sample from the prostate tumor or from a metastasis in a lymph node, bone, liver, lung, or other affected area.

From the sample, somatic testing can provide information about the status of the cancer. It can also help predict whether the cancer could transform into a more aggressive type. And, importantly, targeted therapies (PARP inhibitors) can be used against cancers that have particular molecular tumor biomarkers. Specifically, the testing looks for abnormalities in certain genes involved in DNA repair, including *BRCA1*, *BRCA2*, *ATM*, *PALB2*, *FANCA*, and others.

Tumor stage

The tumor, node, metastasis (TNM) system is used to "stage" prostate cancer. Staging is a way to describe how much cancer is in your body and how far it has spread. Knowing your stage is important for predicting the course of your disease and for making a treatment plan.

In this system, the letters T, N, and M stand for different areas of cancer growth:

- T (tumor) Describes the size of the main (primary) tumor and if it has grown outside the prostate
- N (node) Identifies whether cancer has spread to nearby lymph nodes
- M (metastasis) Indicates if cancer has spread to distant parts of the body (metastasized)

Based on test results, your provider will assign a number to each letter. The higher the number, the larger the tumor (\mathbf{T}) or the more the cancer has spread (\mathbf{M}). These scores are combined to assign a stage to the cancer.

Cancer staging is done when you're first diagnosed. It may also be done after treatment to confirm that the stage hasn't changed.

Measurements and assessments not covered in this book include PSA density, Gleason score, Grade Group, and risk groups. To learn more about these, see the

NCCN Guidelines for Patients: Early-Stage Prostate Cancer, which can be found at <u>NCCN.</u> org/patientguidelines and on the <u>NCCN Patient</u> <u>Guides for Cancer</u> app.



How to read a TNM score

Let's say your prostate cancer is given a TNM score of **T4**, **N1**, **M1**. This score means that the tumor has grown outside the prostate gland (T4) and has spread to nearby lymph nodes (N1) and to one or more distant parts of the body (M1).

Why know your TNM score? For one, it lets you know the extent of your cancer. It also helps characterize your risk. Your level of risk helps indicate the most appropriate treatment for you.

Key points

- Tests are used to plan treatment and check how well treatment is working.
- The prostate gland makes a protein called PSA that helps semen transmit sperm.
- An unusually high amount of PSA in the bloodstream may be a sign of prostate cancer.
- An increase in PSA after treatment may indicate that the treatment is losing effectiveness.
- PSA doubling time indicates how active or aggressive your cancer may be.
- Quality of life refers to your overall satisfaction with your well-being and your ability to participate in regular activities.
- Life expectancy is an estimate of the number of years you will likely live. It's not an exact prediction but it can help choose the best treatment for you.
- Imaging tests are used to see where the cancer has spread beyond the prostate.
 Imaging also shows the size and location of the cancer.
- PSMA-PET imaging locates a protein called prostate-specific membrane antigen (PSMA) on the surface of prostate cancer cells.
- A biopsy is a procedure that removes samples of cells or tissue, which are tested for cancer.
- A genetic test is used to find abnormal changes (mutations) in your genes.

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Be your own advocate. Talk to someone who has gone through the same thing as you. Ask a lot of questions, even the ones you are afraid to ask. You have to protect yourself and ensure you make the best decisions for you, and get the best care for your particular situation."

- An inherited genetic mutation occurs in every cell in your body. A somatic mutation occurs all by itself and is only found in the cells of a tumor.
- To find out if you have an inherited risk for cancer, talk to your doctor about germline testing or ask to be referred to a genetic counselor.
- A biopsy sample of your tumor may be tested to look at its molecular components (somatic testing) for cancer biomarkers.

3 Prostate cancer treatments

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- 34 Supportive care
- 36 Key points

There's more than one treatment for advanced prostate cancer. This chapter describes treatment options and what to expect. Talk with your care team about which treatment might be best for you.

Prostate cancer is a complex disease with many treatment options. Treatments for advanced-stage prostate cancer include hormone therapy as well as non-hormone therapies like chemotherapy, immunotherapy, targeted therapy, and radiation therapy. Often, hormone therapy is combined with one or more other therapies. Combining therapies can be more effective than using either therapy alone.

Hormone therapy

Hormone therapy is a systemic (whole-body) treatment that adds, blocks, or removes hormones. A hormone is a natural chemical made by a gland in the body. Its job is to activate cells or organs.

Male hormones are called androgens. The main androgen is testosterone. Most of the testosterone in the body is made by the testicles. Testosterone helps produce sperm, among other functions. But testosterone also helps prostate cancer grow. A type of hormone therapy called androgen deprivation therapy (ADT) can stop your body from making testosterone or block cancer cells from using testosterone. The key word in ADT is "deprivation"—this therapy "deprives" (starves) the cancer of its main fuel: androgens. This can shrink the tumor or slow tumor growth for a while.

You might hear the term "castration" used when describing prostate cancer or its treatment. This term describes a drastic reduction of testosterone. Castration can be done with hormone-lowering medication or by surgical removal of one or both testicles (orchiectomy). Though orchiectomy is a surgical procedure, it's still considered hormone therapy because it removes the primary source of testosterone: the testicles. While drug hormone therapy can be reversed when the medication is stopped, orchiectomy is permanent and can't be reversed.

Surgical removal of the testicles is much less common nowadays because systemic hormone therapy is often just as effective at blocking testosterone.

What is ADT?

Androgen deprivation therapy (ADT) brings testosterone down to a very low level. Treatments for ADT include:

- LHRH agonist (goserelin, leuprolide, or triptorelin)
- LHRH agonist + anti-androgen (nilutamide, flutamide, or bicalutamide)
- LHRH antagonist (degarelix or relugolix)
- Surgical castration

Hormone therapies for prostate cancer include luteinizing hormone-releasing hormone (LHRH) agonists and LHRH antagonists, both of which cause the testicles to stop making testosterone. You may have heard of leuprolide (Lupron), a commonly used LHRH agonist or degarelix (Firmagon), a commonly used LHRH antagonist. Most LHRH agonists and LHRH antagonists are injections. These may be given monthly, or 2, 3, or 4 times a year. Anti-androgens, corticosteroids, and androgen synthesis inhibitors are available as pills and taken 1 to 3 times a day, depending on the medication. **See Guide 1**.

Newer hormone therapies

Hormone therapy has been the main treatment for advanced prostate cancer for several decades. Longstanding hormone therapies (such as bicalutamide, flutamide, and nilutamide) are sometimes still used for treating prostate cancer. However, newer hormone therapies are better at delaying the

Guide 1 Hormone therapy drugs for prostate cancer		
Anti-androgens block receptors on prostate cancer cells from receiving testosterone.	apalutamide (Erleada), darolutamide (Nubeqa), enzalutamide (Xtandi), bicalutamide (Casodex), flutamide (Eulexin), nilutamide (Nilandron)	
LHRH agonists prevent the release of luteinizing hormone-releasing hormone (LHRH), which causes the testicles to stop making testosterone	goserelin (Zoladex), leuprolide (Lupron Depot, Eligard), triptorelin (Trelstar)	
LHRH antagonists block or stop the pituitary gland (located in the brain) from making LHRH. This causes the testicles to stop making testosterone.	degarelix (Firmagon), relugolix (Orgovyx)	
Androgen synthesis inhibitors block androgen production.	abiraterone (Zytiga), ketoconazole (Nizoral)	
Corticosteroids ("steroids") are synthetic hormones made in a lab that can stop the adrenal glands and other tissues from making testosterone	dexamethasone, hydrocortisone, methylprednisolone, prednisone	

spread of cancer, extending life, and causing fewer side effects.

These newer drugs include abiraterone, apalutamide, darolutamide, and enzalutamide. You may hear your treatment team refer to these as novel, advanced, or next-generation hormone therapies.

Hormone therapy resistance

Hormone therapy can be very effective at shrinking or slowing the growth of your prostate cancer. But for people with metastatic prostate cancer, hormone therapy can lose this effect over time, even when their testosterone is at a very low level. Why? Because the cancer eventually learns how to grow without using testosterone, which makes it unaffected by hormone therapy. The cancer can "resist" the hormone therapy. So this is called hormone-resistant prostate cancer (also called castration-resistant prostate cancer).

It's important to know that prostate cancer that's resistant to hormone therapy is still treatable. Besides non-hormone treatments (such as chemotherapy, targeted therapy, or immunotherapy), other hormone-reducing drugs are available to treat the few cancer cells that aren't yet resistant.

In addition, you'll probably stay on ADT to keep your testosterone at a low level.

Side effects of hormone therapy

Hormone therapy can have significant side effects. Many factors affect your risk for side effects including your age, your health before treatment, how long or often you have treatment, and other things.

Side effects differ among the types of hormone therapy. In general, the longer you're on hormone therapy, the greater your risk of thinning and weakening of your bones (osteoporosis), bone fractures, weight gain, and loss of muscle mass. When you start ADT, you may have a test to measure your bone density. If your bone density is low, your care team can recommend medications you can take.

The sexual side effects of hormone therapy are a significant cause of stress. Hormone

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I was on ADT for 14 months. I had hot flashes several times during the day and usually once at night. I lost my libido, so I had no interest in sex. A year and a half after my ADT ended, my hot flashes were gone and my libido was fully back. I'm glad I chose to have hormone therapy." therapy may reduce your desire for sex and cause erectile dysfunction. Erectile dysfunction means having difficulty or being unable to have an erection of the penis. Erectile dysfunction medicines (such as Viagra and Cialis) aren't usually effective for those on hormone therapy. These drugs don't restore the loss of sexual desire caused by lower androgen levels. However, some treatments that may improve erectile function include injections of medication into the penis, vacuum constriction devices ("penis pump"), or surgical implants that produce an erection.

Your sex drive and your ability to have an erection may gradually return after stopping hormone therapy, though the process may take several months to a year. Some people never regain full ability to have an erection.

It's common to have psychological as well as relationship problems with erectile dysfunction. It's a leading cause of depression in patients with prostate cancer. Ask your care team about therapy or counseling if you're having problems due to erectile dysfunction or symptoms of depression. Help is available.

Other side effects of hormone therapy include tiredness (fatigue), hot flashes, mood changes, weight gain, changes in penis length and testicle size, and tenderness and growth of your breasts.

In addition, hormone therapy increases the risk for diabetes and cardiovascular disease. If you already have either of these conditions, hormone therapy can cause them to get worse. In Black patients, hormone therapy may increase the risk of death from heart issues. Ask your doctor about monitoring your blood pressure and cholesterol levels. Also, let your



Regular exercise can lessen the symptoms and side effects of hormone therapy, including:

- weight gain
- fatigue
- loss of bone and muscle mass

Physical activity can also improve your general health and make you feel better. Ask your care team to recommend an exercise program for you.

primary care physician know you're being treated with ADT.

LHRH agonists can cause a surge in testosterone for a few weeks before dropping to an undetectable level. This increase is called a testosterone flare. A testosterone flare can cause bone pain and urinary problems. But these symptoms will go away after the first few weeks of treatment. You might be given an anti-androgen medicine to prevent testosterone flare.

Talk to your care team about how to manage the side effects of hormone therapy. They have ways to lessen or soothe most of these problems.

Non-hormone therapy

Hormone therapy may be the first treatment recommended for advanced prostate cancer, but it's not the only one. Other systemic treatments that don't use hormones can also slow cancer growth, prevent cancer symptoms, and prolong life.

If you're given non-hormone therapy, you'll likely stay on ADT to make sure your testosterone remains at the lowest possible level. **See Guide 2**.

Chemotherapy

Chemotherapy is a systemic drug treatment that damages rapidly dividing cells throughout the body. Cancer cells divide and multiply rapidly, which makes them a good target for chemotherapy. But chemotherapy can harm healthy cells, too. That's how it can cause side effects. Because chemotherapy can be a tough treatment to go through, it's recommended only for those who are able to physically tolerate it. Despite the side effects, it can help people with metastatic prostate cancer live significantly longer.

Chemotherapy for prostate cancer is a liquid medicine given by intravenous infusion. This means that it's slowly injected into a vein for up to an hour. It's given every 3 weeks for a total of 6 to 10 times (cycles), along with a daily steroid.

Docetaxel

Docetaxel (Taxotere) is the chemotherapy medicine used most often to treat patients with advanced prostate cancer. Though docetaxel can't cure prostate cancer, it can help people live longer as well as reduce their pain and other symptoms. Docetaxel is an option for some who are taking ADT for the first time. Docetaxel is also used to treat metastases after ADT fails to stop cancer growth.

Cabazitaxel

Cabazitaxel (Jevtana) is a chemotherapy option if docetaxel isn't effective. Cabazitaxel can't cure prostate cancer but it can help people live longer and improve pain and other symptoms.

Mitoxantrone

Mitoxantrone (Novantrone) is used to relieve pain and decrease the need for pain medications. It's an option if you aren't able to tolerate other therapies.

Cisplatin and carboplatin

Cisplatin and carboplatin are chemotherapy drugs made from platinum. These are sometimes used for patients with very advanced or aggressive cancer. Usually, either cisplatin or carboplatin is combined with another chemotherapy medicine such as cabazitaxel or docetaxel.

Immunotherapy

The immune system is the body's natural defense against infection and disease. Immunotherapy is a type of systemic therapy that boosts the ability of your immune system to find and destroy cancer cells. Immunotherapy is usually given alone for treating prostate cancer. Immunotherapy drugs include sipuleucel-T and pembrolizumab.

Sipuleucel-T

SipuleuceI-T (Provenge) is intended for those with hormone-resistant metastatic prostate cancer who have few or no symptoms. This drug is known as a "cancer vaccine." First, immune cells are collected from your body and sent to a lab. The immune cells are then activated to identify and target prostate cancer cells. Lastly, the immune cells are injected back into your body where they attack cancer cells.

Pembrolizumab

Pembrolizumab (Keytruda) is a type of immunotherapy called an immune checkpoint inhibitor. For a small percentage of people whose prostate cancer is due to specific genetic mutations, pembrolizumab can restore the immune system's ability to detect and destroy cancer cells.

Гуре of therapy	Brand name	Generic name	Drug form
Chemotherapies	 Taxotere Jevtana Novantrone Platinol Paraplatin 	 docetaxel cabazitaxel mitoxantrone cisplatin carboplatin 	• infusion into a vein
Immunotherapies	ProvengeKeytruda	sipuleucel-Tpembrolizumab	• infusion into a vein
Biomarker-targeted therapies	 Rubraca Lynparza Akeega Talzenna 	 rucaparib olaparib (plus abiraterone) niraparib/abiraterone talazoparib (plus enzalutamide) 	 tablet tablet tablet capsule
Radiopharmaceuticals	PluvictoXofigo	lutetium-177radium-223	• infusion into a vein
Bone-targeted therapies	 Prolia, Xgeva Zometa Fosamax 	 denosumab zoledronic acid alendronate 	injectioninjectiontablet

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Biomarker-targeted therapy

This treatment targets specific biomarkers that are found through molecular tumor testing. Biomarker-targeted therapies are useful only in patients whose prostate cancer is due to specific genetic mutations. This includes mutations in *BRCA1*, *BRCA2*, and other genes that repair damaged DNA. About 1 in 4 patients with metastatic hormone-resistant prostate cancer have this kind of genetic mutation.

Biomarker-targeted therapies (also known as PARP inhibitors) for advanced prostate cancer include rucaparib (Rubraca), olaparib (Lynparza), niraparib and abiraterone (Akeega), and talazoparib (Talzenna). Because genetic mutations differ between people, a treatment that helps one person may not help another.

Radiopharmaceuticals

A radiopharmaceutical is a medicine that contains a radioactive substance. This radioactive substance releases radiation to kill cancer cells. The radiation doesn't travel far from cancer cells so nearby healthy tissue remains mostly unharmed.

Radiopharmaceuticals are injected into a vein (intravenous injection). Because radiopharmaceuticals leave the body through the gut, common side effects are nausea, diarrhea, and vomiting. Radiopharmaceutical drugs include lutetium-177 and radium-223:

Lutetium-177

Lutetium-177 (Pluvicto) is a relatively new radiopharmaceutical that looks for a particular protein (prostate-specific membrane antigen, PSMA) on the surface of prostate cancer cells anywhere in the body. When the drug finds PSMA, it attaches itself to the cancer cells and implants a small amount of its radioactive substance in them. The cancer cells absorb the radiation from the drug and die. Lutetium-177 is an intravenous infusion given once every 6 weeks for up to 6 doses.

Radium-223

Radium-223 (Xofigo) is used to treat prostate cancer that has metastasized in bone but hasn't spread to other organs. Radium-223 collects in bones and gives off radiation that can kill prostate cancer cells there. It's an injection given once a month for 6 months. You'll need to have blood tests before each dose. A bone-targeting therapy, either denosumab or zoledronic acid, is often given with radium-223.

Radium-223 is also used to reduce pain from bone metastases.

Clinical trials

Therapy may also be given as part of a clinical trial. A clinical trial is a type of medical research study. Clinical trials are a key way to assess new treatment approaches. After being developed and tested in a laboratory, potential new ways of fighting cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA).

Everyone with cancer should carefully consider all the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

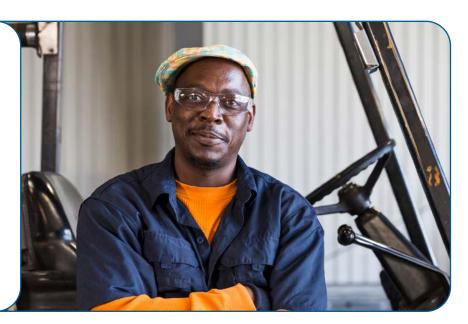
Phases

Most cancer clinical trials focus on treatment. Treatment trials are done in phases.

- Phase 1 trials study the dose, safety, and side effects of an investigational drug or treatment approach. They also look for early signs that the drug or approach is helpful.
- Phase 2 trials study how well the drug or approach works against a specific type of cancer.
- Phase 3 trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- Phase 4 trials study the long-term safety and benefit of an FDA-approved treatment.

Who can enroll?

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



Black males have a higher risk of developing and dying from prostate cancer, but too few are included in clinical trials for new treatments.

NCCN Guidelines for Patients[®] Advanced-Stage Prostate Cancer, 2023 in order to compare how they respond to a specific treatment.

Informed consent

Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. This is an agreement that confirms you've been fully told about your part in the trial. Read the form carefully and ask questions before signing it. Take time to discuss it with family, friends, or others you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

Start the conversation

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

Frequently asked questions

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

Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical

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Finding a clinical trial

In the United States

NCCN Cancer Centers NCCN.org/cancercenters

The National Cancer Institute (NCI) cancer.gov/about-cancer/treatment/ clinical-trials/search

Worldwide

The U.S. National Library of Medicine (NLM) <u>clinicaltrials.gov</u>

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS) 1.800.4.CANCER (1.800.422.6237) <u>cancer.gov/contact</u>

trials. It's common to receive either a placebo with a standard treatment or a new drug with a standard treatment. You'll be informed if a placebo is part of a clinical trial before you enroll.

Are clinical trials free?

There's no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. You may, however, have costs indirectly related to the trial, such as the cost of transportation or childcare due to extra appointments and the costs of routine patient care during the trial. Depending on the trial, you may continue to receive standard cancer care. The standard therapy is billed to—and often covered by—insurance. You're responsible for copays and any costs for this care that aren't covered by your insurance.

Supportive care

Supportive care treats cancer symptoms, the side effects of cancer treatment, and other related health issues. All patients with advanced cancer should be offered supportive care.

Supportive care may be especially useful for patients with bone metastases. Prostate cancer that metastasizes to bones can cause severe pain and fractures (breaks) in bones. Fractures, pain, and bone loss (osteoporosis) can also result from hormone therapy.

Supportive care for bone problems includes:

- Bone-targeted therapy denosumab or zoledronic acid to help prevent fractures
- Palliative radiation therapy for pain symptoms
- Other treatments calcium or vitamin
 D supplements to help prevent fractures

Bone-targeted therapy

Medicines that target bones can help to relieve bone pain and reduce the risk of bone problems. Some medicines work by slowing or stopping bone breakdown, while others help increase bone thickness.

Some treatments for prostate cancer, like hormone therapy, can cause osteoporosis and increase your risk of fractures. Also, cancer that spreads to your bones puts them at risk for injury and disease. Such problems include osteoporosis, fractures, bone pain, and squeezing (compression) of the spinal cord.

If you're at risk for osteoporosis, you may have a bone mineral density test. This is a special x-ray scan that measures how much calcium and other minerals are in your bones. Bone mineral density tests look for osteoporosis and help predict your risk for bone fractures. You should have a follow-up bone mineral density test after 1 year of hormone therapy. You might also have blood tests to monitor kidney function and calcium levels.

Drugs to prevent bone loss and fractures include Prolia (denosumab), Xgeva (denosumab), Zometa (zoledronic acid), and Fosamax (alendronate).

For more information about supportive care, see chapter 6.

Shared decision-making

Some people with cancer want their doctors and treatment team to just tell them which treatment to have. Doctors, nurses, and other providers are the experts, right? While it's true that your treatment team has lots of experience and knowledge, you're also an expert—you're the expert on you.

It's a good idea for your team to share the responsibility of your treatment with you. And it's a good idea for you to fully participate in making decisions about your care.



Here's what your treatment team should share with you:

- An explanation of the likely benefits and potential harms of each treatment option.
- The likelihood of cure, recurrence, progression, and possible mortality with each treatment option.
- The side effects of each treatment option along with their impact on quality of life, including sexual, urinary, and bowel function.

And here's what you should share with your treatment team:

- Your preferences and feelings about treatment, side effects, risks, and quality of life. These should be key parts of your treatment plan.
- If the provider who's leading your treatment team doesn't have a talk with you about shared decision-making, feel free to speak up and ask about it.

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Key points

- Hormone therapy is often combined with one or more other therapies, which can be more effective together at slowing or shrinking advanced prostate cancer.
- > Testosterone helps prostate cancer grow.
- Androgen deprivation therapy (ADT) treats prostate cancer by stopping testosterone from being made or by blocking cancer cells from using testosterone.
- Castration describes a drastic reduction of testosterone. This can be done surgically or with drugs.
- Newer hormone therapies are better at delaying the spread of cancer, helping people live longer, and causing fewer side effects.
- Hormone therapy can eventually lose its effectiveness against prostate cancer. This becomes hormone-resistant prostate cancer.
- Hormone therapy can cause many side effects. Sexual side effects of hormone therapy are a significant cause of stress but treatment and therapy are available.
- Shared decision-making combines the treatment team's knowledge and experience with your preferences and values.
- Chemotherapy is used with hormone therapy in patients with advanced prostate cancer. It can slow cancer growth and help people live longer.

- Among chemotherapy medicines, docetaxel is the one used most often to treat patients with advanced prostate cancer.
- Immunotherapy helps the immune system to detect and destroy cancer cells.
- Biomarker-targeted therapies are useful for patients whose prostate cancer is due to specific genetic mutations.
- A clinical trial studies a treatment to see how safe it is and how well it works.
 Sometimes a clinical trial is the preferred treatment option for prostate cancer.
- Supportive care relieves the symptoms caused by cancer and the side effects caused by its treatment.
- Everyone with advanced-stage prostate cancer should be offered supportive care.

4 Regional prostate cancer treatment options

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- 38 Treatment
- 41 Follow-up after treatment
- 42 Treatment for persistence or recurrence
- 42 Now what?
- 44 Key points

Regional prostate cancer has grown outside the prostate gland to nearby areas like lymph nodes, but not any farther. It usually requires both local and systemic (whole-body) treatment.

About regional prostate cancer

Regional prostate cancer is cancer that has spread from the prostate gland to neighboring tissue, such as nearby lymph nodes, the bladder, or the rectum. But it hasn't spread any farther. (To read about prostate cancer that has spread to distant lymph nodes, bones, or organs, turn to chapter 5.) Regional prostate cancer is also sometimes called locally advanced prostate cancer.

Treatment

The key concern about prostate cancer that spreads just outside the prostate is that it could continue to spread farther (metastasize) to other areas of the body. As a result, treatment for regional prostate cancer is more aggressive than treatment for early-stage prostate cancer.

Treatment takes aim at cancer in the prostate itself as well as cancer outside the prostate. So it often includes both local therapy (radiation therapy or prostate surgery) and systemic therapy (hormone therapy). Treatment options are also based on life expectancy and symptoms. The longer the life expectancy and the more symptoms, the more aggressive the treatment. **See Guide 3.**

Life expectancy: More than 5 years or you have symptoms

If your life expectancy is more than 5 years or you have symptoms, treatment usually includes:

Radiation therapy

Radiation therapy uses high-energy rays, like x-rays or gamma rays, to kill cancer cells and shrink tumors. Radiation therapy is given in regular doses over a certain period of time.

External beam radiation therapy (EBRT) is the type of radiation used for prostate cancer. EBRT uses a machine that aims radiation precisely at cancer inside the body. The radiation beam focuses directly on the cancer while trying to avoid healthy tissue. This technique delivers higher doses of radiation more safely.

EBRT along with long-term hormone therapy plus abiraterone (Zytiga) is the preferred initial treatment for patients who have regional prostate cancer and a longer life expectancy or symptoms. Preferred treatments are ones that have the most scientific evidence that they work well.

EBRT treats the prostate as well as cancerous lymph nodes, while long-term hormone therapy lowers testosterone to a minimal level to prevent the cancer from getting worse. Longterm hormone therapy is given before, during, and after EBRT for 2 to 3 years. Radiation therapy is also used as palliative treatment to relieve the pain of bone metastases.

Some of the common side effects of radiation therapy are urinary and bowel problems, erectile dysfunction, and fatigue.

Hormone therapy

Long-term hormone therapy consists of androgen deprivation therapy (ADT) plus abiraterone, an androgen inhibitor. If you're taking abiraterone, you'll also need to take a steroid to reduce abiraterone's side effects.

Another option for initial treatment is radiation therapy plus long-term (2 to 3 years) ADT without the addition of abiraterone. This may be an option for those who can't take abiraterone due to other health conditions. ADT on its own is an option for patients with regional prostate cancer who have other significant or life-threatening health problems. Abiraterone can be added to ADT, which may help patients live longer although it may also come with more side effects.

Prostate surgery

Prostatectomy means removing the prostate gland through surgery. A radical prostatectomy removes not only the entire prostate but also the surrounding tissue and seminal vesicles. A pelvic lymph node dissection (PLND) is an operation to remove the nearby lymph nodes.

A radical prostatectomy with PLND is a treatment option only in certain cases of regional prostate cancer. It's used when:

> The tumor is found only in the prostate.

Life expectancy	Treatment			
	EBRT with ADT + abiraterone + steroid (preferred)			
	EBRT with ADT			
More than 5 years or	ADT with or without abiraterone			
you have symptoms		Additional treatment:		
	Radical prostatectomy and dissection of pelvic lymph nodes	 EBRT with or without ADT ADT with or without EBRT Monitoring 		
	Observation			

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Regional prostate cancer treatment options » Treatment

- The tumor can be removed completely with surgery.
- You have a life expectancy of 10 or more years.
- You have no other serious health conditions.

A radical prostatectomy is complex and requires a great deal of skill. Surgeons who are experienced in this type of surgery often have better results. Sometimes cavernous nerve bundles are damaged or removed during surgery. The cavernous nerves control the ability to have erections. These nerves run alongside the prostate. Surgeons do their best to avoid these nerves when performing a prostatectomy, but damage to the nerves during surgery is sometimes unavoidable.

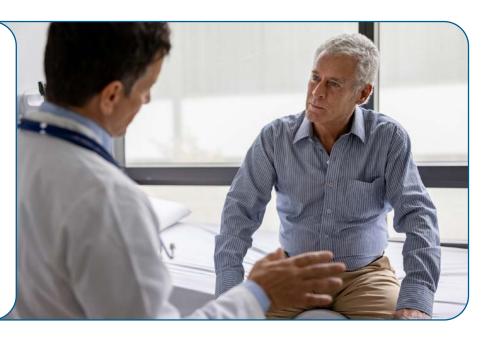
Because the surgeon is able to see inside you during prostate surgery, it often reveals more details about your disease. It could show that the cancer has spread to nearby lymph nodes.



I had a radical prostatectomy. Because my prostate cancer was very close to one nerve bundle, I chose to have it removed also. I wasn't troubled by this because I learned that there are other ways of getting erections. I wanted to live to see my grandchildren grow up, and now they have!"

Or there may be other signs of cancer after the prostate is removed. In either case, you might have additional treatment at some point after the surgery. If there are signs of remaining cancer but no metastasis in lymph nodes, additional treatment involves EBRT with or

About 1 in 8 people with prostate cancer are diagnosed with regional prostate cancer.



without added hormone therapy. If there is metastasis in lymph nodes, treatment involves ADT with or without EBRT. Or your care team may suggest that you delay additional treatment until signs or symptoms (such as a rising PSA level) begin to occur.

Side effects of radical prostatectomy include urinary incontinence and erectile dysfunction.

Urinary incontinence (being unable to hold your urine) is usually temporary. Most patients gradually recover control of their bladder after a few months or so. Doing exercises to strengthen the pelvic floor can help. If incontinence continues to be a problem, another surgical procedure can be done to improve it.

Erectile dysfunction means having difficulty or being unable to have an erection of the penis. It may take several months to 2 years to restore the erectile function you had before the surgery. However, you may never regain the same erectile function you once had. Treatment options include pills (like Viagra and Cialis), injections of medication into the penis, vacuum constriction devices ("penis pump"), and surgical implants that produce an erection.

It's common to have psychological as well as relationship problems with erectile dysfunction. It's a leading cause of depression in patients with prostate cancer. Ask your care team about therapy or counseling if you're having any problems due to erectile dysfunction or any symptoms of depression. Help is available.

Life expectancy: 5 years or less and no symptoms

Treatment is less aggressive for people with regional prostate cancer whose life expectancy is 5 years or less and who have no symptoms:

ADT

ADT on its own is an option for patients with regional disease, no symptoms, and life expectancy of 5 years or less. It's used to slow cancer and delay or reduce symptoms. ADT may include an LHRH agonist, an LHRH antagonist, or surgical removal of the testicles.

Observation

Observation is another option for patients with a life expectancy of 5 years or less. It's for those with other serious health problems whose prostate cancer isn't causing any symptoms. Observation involves occasional PSA tests and watching for symptoms, which can be treated with pain-relieving (palliative) therapy.

Follow-up after treatment

After initial treatment, you'll have follow-up tests to find out how well your therapy worked. Periodic PSA tests and occasional imaging scans can indicate whether the cancer is under control.

PSA is very low or undetectable

If your PSA is very low after radiation therapy or undetectable after prostate surgery, you'll be monitored for cancer recurrence. Monitoring involves PSA testing every 6 to 12 months for several years. Patients with a high risk of recurrence may have PSA testing more often, such as every 3 months. You'll continue to be monitored on an ongoing basis or until signs or symptoms occur.

PSA is elevated or rising

If your PSA doesn't fall to an undetectable level after prostate surgery, you may still have cancer (persistence). Or, if your PSA drops after initial treatment but then later rises again, it probably means the cancer has come back (recurrence). In either case, further treatment is available.

Treatment for persistence or recurrence

If you have PSA resistance or PSA recurrence after your initial therapy, your life expectancy will guide what treatment you may have next.

More than 5 years

Before deciding on any treatment, you'll need some more tests to find out how aggressive the cancer may be. Tests include PSA doubling time; imaging with CT, MRI, or whole-body PET scan; and possibly a biopsy. Results of these tests will indicate your next treatment.

In addition, treatment for cancer persistence or recurrence is based on whether your initial treatment for regional prostate cancer was radiation therapy or prostate surgery. **See Guide 4.**

5 years or less

If your life expectancy is 5 years or less, observation may be a better option than undergoing treatment. Observation involves

NCCN Guidelines for Patients[®] Advanced-Stage Prostate Cancer, 2023 checking up on your prostate cancer and watching for symptoms. If symptoms develop, treatment is often focused on easing or stopping them instead of trying to cure the cancer. This allows patients to maintain a good quality of life without the burden of unnecessary treatment.

Now what?

After you've been treated for regional prostate cancer, and perhaps PSA persistence or PSA recurrence, you'll continue to have tests and visits to treat your existing cancer or to watch out for cancer to return.

Surveillance is a key part of your follow-up plan. Be sure to continue to go to follow-up visits, have your PSA tested regularly, and stay in touch with your treatment team. As always, you can ask to join a clinical trial.

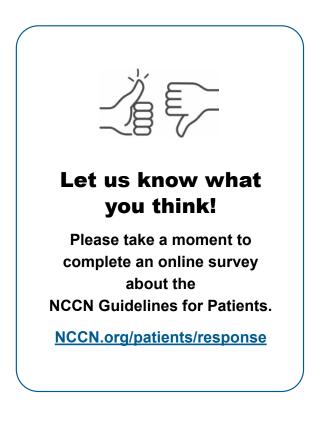
Guide 4 Treatment for PSA persistence or PSA recurrence				
	Test results	Treatment options		
	No other signs of cancer	 Radiation therapy with or without hormone therapy Monitoring 		
PSA persistence/recurrence after radical prostatectomy	Cancer in prostate bed or pelvis	 Radiation therapy and hormone therapy, with or without abiraterone 		
	Cancer has spread to another area of the body (metastasized)	Advanced treatment required		
	No other signs of cancer	MonitoringHormone therapy		
PSA recurrence after	Cancer in prostate	 Monitoring Radical prostatectomy with dissection of pelvic lymph nodes Brachytherapy Cryotherapy High-intensity focused ultrasound 		
radiation therapy	Cancer in pelvis	 Monitoring Hormone therapy Radiation therapy of pelvic lymph nodes (only if not done before) Dissection of pelvic lymph nodes 		
	Cancer has spread to another area of the body (metastasized)	 Advanced treatment required 		

NCCN Guidelines for Patients[®] Advanced-Stage Prostate Cancer, 2023

Key points

- Regional prostate cancer has spread from the prostate gland to neighboring tissue, but no farther.
- The main concern about regional prostate cancer is that it could continue to spread to other areas of the body.
- Treatment for regional prostate cancer often includes both local therapy and systemic therapy.
- Radiation kills cancer cells or stops new cancer cells from being made. External beam radiation therapy (EBRT) is the type of radiation used for prostate cancer.
- The preferred initial treatment for regional prostate cancer in people with a longer life expectancy or symptoms is EBRT, long-term ADT, and abiraterone
- A radical prostatectomy is a surgical procedure that removes the whole prostate, the surrounding tissue, the seminal vesicles, and sometimes the nearby lymph nodes in the pelvis.
- Erectile dysfunction can lead to psychological problems (such as depression) and relationship difficulties. Help is available.
- Treatment is less aggressive for people with regional prostate cancer whose life expectancy is 5 years or less and who have no symptoms.
- After initial treatment for regional prostate cancer, patients will have periodic PSA tests to check whether the cancer is under control.

- PSA persistence is when your PSA doesn't fall to an undetectable level. This indicates the cancer hasn't gone away.
- PSA recurrence is when your PSA level drops after initial treatment but rises again. This indicates the cancer has come back.



5 Metastatic prostate cancer treatment options

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- 54 Now what?
- 55 Key points

When prostate cancer spreads to other parts of the body, then systemic (whole-body) therapy is needed. This chapter explains the treatment options for distant metastatic prostate cancer.

About metastatic prostate cancer

Metastatic prostate cancer is cancer that has spread (metastasized) outside the prostate and beyond the pelvis to other areas of the body. Areas where prostate cancer tends to spread are:

- Lymph nodes farther away from the prostate
- > Bones in the spine, pelvis, or ribs
- Organs such as the liver, lungs, brain, or others

You may have metastatic cancer when you're first diagnosed. Or your cancer may become metastatic after you've already had treatment for early-stage or regional prostate cancer.

Metastatic prostate cancer can be difficult to treat. However, a variety of therapies are available to target the cancer, stop or slow its progress, and reduce symptoms.

"When you are deciding on your treatment options, remember that even though some decisions need to be made fast, don't rush. Think through your options and get second, or even third opinions. Have people you can trust to talk through your options so you feel comfortable in your decisions."



NCCN Guidelines for Patients[®] Advanced-Stage Prostate Cancer, 2023

Main treatment

The main treatment for metastatic prostate cancer is hormone therapy, specifically androgen deprivation therapy (ADT).

The aim of ADT is to reduce androgens (mostly testosterone) to a point where they don't provide fuel for the cancer. This low point is called castration level, which is when there's less than 50 ng/dL of testosterone in the bloodstream. Patients whose metastatic prostate cancer is newly diagnosed will begin ADT to get to castration level. Patients with metastatic prostate cancer who are already being treated with ADT will continue the treatment to keep testosterone at a minimal level.

ADT comes in a few forms. These include drugs (an LHRH agonist with or without an anti-androgen, or an LHRH antagonist) or sometimes surgery (removal of the testicles).

Although ADT is the main therapy for advanced prostate cancer, it's not usually given on its own any more. Adding one or two additional therapies to ADT may help you live longer and with fewer symptoms. You may hear this called doublet therapy (ADT + another therapy) or triplet therapy (ADT + two additional therapies). Additional therapies include second hormone therapy, chemotherapy, immunotherapy, targeted therapy, and radiopharmaceuticals.

Which additional therapy you'll have depends on a number of considerations. The first consideration is whether ADT is still effective for you.

Hormone-resistant prostate cancer

(also called castration-resistant prostate cancer) is cancer that learns how to grow without using testosterone as its fuel. As a result, hormone therapy is no longer as effective against it—the cancer becomes "resistant" to ADT. If you've had ADT but it's not working well any more, go to page 49 to read about treatment options for hormoneresistant metastatic prostate cancer.

Hormone-sensitive prostate cancer

(also called castration-sensitive prostate cancer) is not currently being treated with ADT or has never been treated with ADT. (This **doesn't** include ADT given as shortterm additional therapy, such as hormone therapy given during radiation therapy.) As a result, this cancer is "sensitive" to hormone therapy. That is, hormone therapy can still treat it. You may also hear it called by its former name castration-naïve prostate cancer, which means that hormone therapy is a new ("naïve") treatment for the cancer. If this describes your cancer, read the following section about treatment options for hormone-sensitive prostate cancer.

Hormone-sensitive treatment

As its name implies, hormone-sensitive metastatic prostate cancer is treated mainly with hormone therapy. ADT is considered the first hormone therapy. But a second hormonereducing therapy is commonly added to ADT for treating advanced prostate cancer. It can prevent your cancer from growing and spreading farther. **See Guide 5.**

Preferred treatments

Preferred treatments are ones that have the most scientific evidence that they work well. Preferred treatment options for hormonesensitive prostate cancer include ADT plus a second hormone-reducing medicine. Medical research has shown that patients on ADT plus another hormone-reducing medicine tend to live longer than those on ADT alone. The preferred second hormone-reducing medicines are abiraterone, apalutamide, and enzalutamide. Your care team will talk to you about which medicine might work best for you.

If you're prescribed abiraterone, you'll also be given a steroid medication. The steroid helps reduce the side effects of abiraterone.

Other preferred treatments for hormonesensitive metastatic prostate cancer are triplet therapy options: ADT plus a chemotherapy medicine (docetaxel) plus a hormone-reducing medicine (either abiraterone or darolutamide). This adds up to a lot of medicine. So triplet therapy is only recommended for people who have high-volume prostate cancer who also can physically tolerate chemotherapy while on hormone therapy, plus other treatment. Highvolume prostate cancer means having multiple

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Treatment options for hormone-sensitive prostate cancer

	ADT +	abiraterone (Zytiga) + steroid	
	ADT +	apalutamide (Erleada)	
Preferred options	ADT +	enzalutamide (Xtandi)	
	ADT + chemotherapy	abiraterone (Zytiga) + steroid	
	(docetaxel) +	darolutamide (Nubeqa)	
Other options	ADT +	radiation therapy (EBRT)	
Other options	ADT alone		

metastases in bones and/or at least one metastasis in an internal organ.

Other treatments

Low-volume prostate cancer means having zero to a few metastases in bones and/or some metastases in distant lymph nodes, with no metastases in internal organs. For patients with low-volume hormone-sensitive prostate cancer, ADT plus external beam radiation therapy (EBRT) to the metastases is recommended to help stop the cancer from spreading farther.

ADT used by itself is usually not recommended, except for patients who aren't able to handle side effects or take other medicines.

Follow-up visits

After treatment, you'll have follow-up tests on a regular basis to see how well the treatment is working and to check for any signs or symptoms that the cancer has returned.

If follow-up tests find that treatment isn't working and your hormone-sensitive prostate cancer is growing or spreading, then you may have developed hormone-resistant prostate cancer. This is discussed next.

Hormone-resistant treatment

Hormone-resistant metastatic prostate cancer is cancer that keeps growing even when testosterone is at a very low level. How? Some cancer cells learn to survive without the usual supply of testosterone. Also, the cancer may get some androgens from the adrenal glands, which make a small amount of testosterone. Even the tumor itself can create androgens that help cancer cells grow. As these cells multiply, ADT gradually loses its effectiveness against the cancer.

ADT

To treat hormone-resistant metastatic prostate cancer, your testosterone needs to remain at castration level. So it's still important to stay on ADT. Your care team may keep you on your same ADT treatment or might ask you to switch to a different medicine.

Besides ADT, your care team will recommend additional treatment. **See Guide 6.** Which treatment you'll receive will depend on a few factors. These include:

- Your previous treatment (if any)
- Location of the metastasis in your body
- > Amount of metastatic disease
- > Symptoms
- Potential side effects
- > Your preferences

In addition to ADT, treatments for hormoneresistant metastatic prostate cancer include second hormone therapy, chemotherapy, immunotherapy, biomarker-targeted therapies, and radiopharmaceuticals—or a combination of these treatments.

If you were first diagnosed with early prostate cancer or hormone-sensitive prostate cancer, then you may have already had ADT and chemotherapy or next-generation hormone therapy. Having had either of these therapies will affect which treatment you'll have next.

Second hormone therapy

ADT is the first hormone therapy used for treating metastatic prostate cancer. If prostate cancer becomes hormone resistant, then a second hormone therapy is commonly added. A second hormone therapy may be able to slow down your cancer or keep it from spreading farther. The preferred second therapy options include newer (nextgeneration) hormone therapies:

- abiraterone (Zytiga)
- enzalutamide (Xtandi)

Other second hormone therapy

If the preferred second hormone therapies don't slow down your cancer, there are other hormone-reducing options:

- Adding one of the early-generation antiandrogens (nilutamide, flutamide, or bicalutamide) may be effective if newer hormone therapies aren't an option due to cost or availability.
- Stopping an anti-androgen may also be effective. Sometimes stopping the drug has the opposite effect of lowering PSA levels in some patients.
- NCCN Guidelines for Patients[®] Advanced-Stage Prostate Cancer, 2023

- A corticosteroid (hydrocortisone, prednisone, or dexamethasone) can be a hormone-reducing therapy itself when used in addition to ADT.
- Ketoconazole (Nizoral) is a pill that's occasionally prescribed when second hormone therapy or chemotherapy can't be used or isn't available. It's taken with a steroid (hydrocortisone) to reduce side effects such as nausea and vomiting.

Chemotherapy

ADT plus chemotherapy can be the first treatment for metastatic prostate cancer or it can be given later if other treatments haven't worked well. Chemotherapy can be given as a single drug (such as docetaxel) or as a pair (cabazitaxel and carboplatin) if the cancer is more aggressive. Docetaxel (Taxotere) is the preferred chemotherapy. You'll also take a steroid (prednisone or dexamethasone) to reduce the side effects of chemotherapy.

Chemotherapy options include:

- docetaxel (Taxotere)
- cabazitaxel (Jevtana)
- cisplatin (Platinol)
- carboplatin (Paraplatin)
- mitoxantrone (Novantrone)

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Treatment options for hormone-resistant prostate cancer

	Type of therapy	Treatment		therapy Treatment When to use		When to use
	Second hormone therapy	ADT +	abiraterone (Zytiga) + steroid	Initial therapy		
Preferred options		ADT +	enzalutamide (Xtandi)	Initial therapy		
	Chemotherapy	ADT +	docetaxel (Taxotere) + steroid	Initial therapy		
		ADT +	anti-androgen (start one or stop one)	Only if you've already had initial therapy		
Other options	Second hormone therapy	ADT +	corticosteroid	Only if you've already had initial therapy		
		ADT +	ketoconazole (Nizoral) + hydrocortisone	Only if you've already had initial therapy		
	Immunotherapy	ADT +	sipuleucel-T (Provenge)	Only if few or no symptoms and if treated with hormone therapy or chemotherapy		
	Targeted therapy	ADT +	olaparib (Lynparza) + abiraterone (Zytiga) + steroid	Only if a <i>BRCA</i> mutation and before hormone therapy or chemotherapy		
Specific options	Targeted therapy	ADT +	olaparib (Lynparza)	Only if a DNA-repair gene mutation and if treated with hormone therapy		
options	Targeted therapy	ADT +	rucaparib (Rubraca)	Only if a <i>BRCA</i> mutation and if treated with hormone therapy and chemotherapy		
	Targeted therapy	ADT +	niraparib/abiraterone (Akeega) + prednisone	Only if a <i>BRCA</i> mutation		
	Targeted therapy	ADT +	talazoparib (Talzenna) + enzalutamide	Only if a <i>BRCA</i> or other DNA-repair gene mutation		
				Continues on next page		

Guide 6 *(continued)* Treatment options for hormone-resistant prostate cancer

Continued from previous page

	Type of therapy		Treatment	When to use
	Chemotherapy	ADT +	cabazitaxel (Jevtana) + steroid	Only if previously treated with docetaxel
	Chemotherapy	ADT +	cabazitaxel (Jevtana) + carboplatin + steroid	Only if aggressive metastatic cancer or more than one genetic mutation
Specific	Chemotherapy	ADT +	mitoxantrone (Novantrone) + prednisone	For reducing pain in patients who can't take other therapies and if treated with docetaxel
options	Radiopharmaceutical	ADT +	radium-223 (Xofigo)	For reducing pain of bone metastases
	Radiopharmaceutical	ADT +	lutetium-177 (Pluvicto)	Only with PSMA/PET imaging and if treated with hormone therapy and docetaxel
	Immunotherapy	ADT +	pembrolizumab (Keytruda)	Only if you have certain genetic mutations and there are no other treatment options

Immunotherapy

Immunotherapy drugs boost the body's own immune system to fight cancer. However, immunotherapy for prostate cancer is used only for certain patients. Immunotherapy drugs include:

Sipuleucel-T (Provenge) can be used for patients whose hormone-resistant metastatic prostate cancer is causing few or no symptoms. Such patients usually have less cancer and a stronger immune system, which allows this immunotherapy to be more effective. Sipuleucel-T is not recommended for those whose prostate cancer has spread to internal organs.

Pembrolizumab (Keytruda) is recommended only for patients whose hormone-resistant metastatic prostate cancer has grown or spread despite having chemotherapy and second hormone therapy. Patients' test results will also show specific genetic changes (defects in DNA called deficient mismatch repair and high microsatellite instability).

Targeted therapy

Biomarker-targeted therapies are useful only in patients whose hormone-resistant metastatic prostate cancer is linked with specific genetic mutations. These drugs target mutations in genes that repair damaged DNA. Biomarkertargeted therapies include:

- Olaparib (Lynparza) plus abiraterone and a steroid can be used for patients with a BRCA mutation before having second hormone therapy or chemotherapy.
 Olaparib may also be used for patients whose metastatic cancer has grown or spread after second hormone therapy (abiraterone or enzalutamide) and who have a mutation in a BRCA gene or other gene that repairs DNA.
- Rucaparib (Rubraca) can be used for patients with a BRCA mutation whose cancer has already been treated with both second hormone therapy and chemotherapy (docetaxel or cabazitaxel).
- Niraparib and abiraterone (Akeega) plus prednisone is a new targeted therapy for patients with a *BRCA* mutation. Patients should also be on an LHRH agonist, LHRH antagonist, or have had orchiectomy (surgical removal of the testicles).
- Talazoparib (Talzenna), taken with enzalutamide (Xtandi), is another new targeted therapy for patients with a mutation in a *BRCA* or other DNA-repair gene.

Radiopharmaceuticals

If your initial or other treatments haven't worked well, your care team may suggest a radiopharmaceutical drug.

- Lutetium-177 (Pluvicto) isn't used until after both a second hormone therapy and chemotherapy (docetaxel or cabazitaxel) have been given. First, you'll have PSMA-PET imaging to confirm the treatment could work.
- Radium-223 (Xofigo) can be used if prostate cancer has spread mainly to bones but not to internal organs. It should only be used in combination with ADT, not with second hormone therapy or chemotherapy.

Clinical trial

Participating in a clinical trial is often an option. You can try to join a clinical trial at any time. You don't need to wait until you've "run out of other options."

Supportive care

Supportive care for patients with bone metastases includes:

- Bone-targeted therapy Denosumab or zoledronic acid to help prevent fractures
- Palliative radiation therapy Direct radiation to painful bone tumors or tumors that interfere with bodily functions
- Other treatments Calcium or vitamin
 D supplements to help prevent fractures

Follow-up visits

After treatment, you'll have follow-up tests on a regular basis to see how well the treatment is working and if there are any side effects from treatment. Tests include:

- Physical exam with PSA test every 3 to 6 months or more often
- Imaging if cancer symptoms occur
- Imaging as needed to look for cancer growth or spread

No growth or spread

If the cancer doesn't grow or spread, your current treatment may be keeping your cancer in check. Your provider will continue to give you tests. If your situation remains stable, you'll stay on your current treatment unless changes or symptoms begin to occur.

Growth or spread

If your cancer grows or spreads, your treatment team may suggest you retry a therapy you've had before, or begin a new and different therapy. Many patients with advanced prostate cancer eventually receive two, three, or more different therapies in the course of their treatment.

If possible, consider all the treatment options. Talk with your team about what you want from treatment. You may ask for a second opinion before you start another therapy. You can explore any clinical trials that are available. And you always have the option to stop systemic therapy.

You'll continue to be offered supportive care.

Now what?

Surveillance is a key part of your follow-up plan. Be sure to continue to go to follow-up visits and stay in touch with your treatment team.

It's common to feel frustration, anger, regret, despair, and uncertainty—even all at the

Many patients with advanced prostate cancer eventually receive two, three, or more different therapies in the course of their treatment.



NCCN Guidelines for Patients[®] Advanced-Stage Prostate Cancer, 2023 same time. Know that you can have prostate cancer and still find happiness after diagnosis and treatment. Try to enjoy life as much as possible. Talk with family or friends. Join a support group to learn how other patients are dealing with their cancer. Or talk to your doctor or another member of your care team. They can point you to professionals who can help you deal with these feelings and guide you toward your next steps.

Key points

- Metastatic prostate cancer has spread outside the prostate and beyond the pelvis to other areas of the body, such as distant lymph nodes, bones, or organs.
- The first treatment for advanced metastatic prostate cancer is usually ADT. Adding another therapy or two to ADT may help you live longer and with fewer symptoms.
- Hormone-sensitive prostate cancer is treated mainly with hormone therapy.
- Hormone-resistant prostate cancer has learned how to grow without using testosterone as its fuel. It's treated with ADT and another type of therapy—often a newer hormone therapy or chemotherapy.
- High-volume prostate cancer means having multiple metastases in bones and/ or at least one metastasis in an internal organ.
- Low-volume prostate cancer means having zero to a few metastases in bones and/or some metastases in distant lymph nodes, with no metastases in internal organs.

- Second hormone therapy is commonly added to ADT as a preferred treatment option for advanced prostate cancer.
- Targeted therapies are useful only in patients whose prostate cancer is linked with specific genetic mutations.
- If your initial treatments haven't worked well or aren't working as well as they did before, your care team may suggest a radiopharmaceutical drug.
- During or after your treatment, your care team will watch you closely to see how well the treatment is working and to look for any treatment side effects.
- Many patients with advanced prostate cancer eventually receive two, three, or more different therapies in the course of their treatment.
- Prostate cancer and its treatment may cause you to feel frustration, anger, regret, despair, and uncertainty. Know that you can still find happiness after diagnosis and treatment.

6 Supportive care and other assistance

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- 61 Key points

NCCN Guidelines for Patients® Advanced-Stage Prostate Cancer, 2023 Supportive care addresses the symptoms and side effects of prostate cancer, as well as psychological, social, financial, and spiritual issues. Many resources are available to help you feel better and answer your questions.

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

Supportive care

Supportive care is for relieving the symptoms of cancer, the side effects of cancer therapies, and other health issues related to the cancer. Supportive care also helps with psychological, social, and spiritual issues.

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

Supportive care involves the whole person, not just their cancer. Supportive care addresses many needs. It can help with making treatment decisions. It can also assist with coordinating care between health providers. Notably, supportive care can help prevent or treat physical and emotional symptoms. Supportive care can also help with financial support, advance care planning, and end-of-life concerns.

It's important to talk openly with your treatment team about supportive care. Some medical centers have patient navigators or other staff members who coordinate nonclinical supportive care. Ask questions and reach out if you need more information about supportive care.

Anxiety and depression

Many people with prostate cancer experience symptoms of distress, such as anxiety and depression. You may feel anxious during testing, or you may experience depression during a hard part of treatment, or because your life is not the same as it was before cancer. Tell your treatment team if you're experiencing these symptoms so that you can get help.

"

Report any unusual feelings of sadness, loss of interest in activities, anxiety, and sleep problems to your doctor. Many people experience these feelings, and they should not go untreated."

Supportive care and other assistance » Support groups » Financial concerns

Help can include support groups, talk therapy, or medication. At your cancer center, patient navigators, social workers, and other experts can help. Some people also feel better by exercising, talking with loved ones, or relaxing.

Support groups

Many people diagnosed with cancer find support groups to be helpful. A support group provides the opportunity to talk with others who are going through, or have been through, similar experiences. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn't have support groups for people with cancer, have a look at the online resources listed on page 72 of this book.

Financial concerns

The financial cost of prostate cancer can be overwhelming. As a result, many people with prostate cancer and their loved ones struggle with the cost of treatment, as well as the stress of paying for it.

To make things worse, you may miss work during treatment or become unemployed. Or you may have trouble paying for or getting medicines. Or you may have too little or no health insurance.

If you struggle to pay for food, housing, treatment, follow-up care, and other expenses, or you have difficulty getting to appointments, talk with your care team's social worker, patient navigator, and hospital financial services staff.



It's important to ask for help

Depression, anxiety, fear, and distress are very common feelings for people with cancer. These feelings can make it harder to deal with cancer and cancer treatment. They can hold you back even when you want to move forward.

Getting help when you're feeling worried or hopeless is an important part of cancer care. If you're feeling anxious or overwhelmed, ask your treatment team for help.

More information about cancer and distress is available at <u>NCCN.org/</u> <u>patientguidelines</u> and on the <u>NCCN</u> Patient Guides for Cancer app.

They can help you find financial support and transportation options.

You can also talk to your treatment team about work, health insurance, or money problems. Your team can include information in your treatment plan to help you manage your finances and medical costs. If your doctors and care providers don't talk about how to pay for treatment, it's OK for you to ask them about it first.

Survivorship

Survivorship focuses on the health and wellbeing of a person with cancer from diagnosis until the end of life. This includes the physical, mental, emotional, social, and financial effects of cancer that begin at diagnosis, continue through treatment, and arise afterward.

Survivorship also includes concerns about follow-up care, late effects of treatment, cancer recurrence, and quality of life. Support from family members, friends, and caregivers is also an important part of survivorship.

Read more about survivorship in NCCN Guidelines for Patients: Survivorship Care for Healthy Living and Survivorship Care for Cancer-Related Late and Long-Term Effects, available at <u>NCCN.org/patientguidelines</u> and on the <u>NCCN Patient Guides for Cancer</u> app.





Advance care planning

When cancer is diagnosed at an advanced stage or keeps progressing despite all treatment efforts, it may be time to consider what lies ahead. Even when cancers are curable, talking about future scenarios should begin when starting treatment. This exploration of what's important to you is called advance care planning.

Consider quality of life

Quality of life is a term used often in cancer care. It refers to a person's overall enjoyment of life, including their sense of well-being and ability to participate in regular activities. For some people, aggressive cancer treatment may extend their life but reduce their quality of life. That's one reason why quality of life should be an important consideration when making decisions about cancer treatment.

Advance care planning is for everyone, not just for those who are very sick. Advance care planning means deciding what care you would want if you become unable to make medical decisions for yourself. It's about making sure that your wishes are understood and respected.

The focus is on you receiving the best possible care at the end of your life. Patients with incurable cancer can set up an advance care plan early to help them feel less stressed and better able to cope with their condition.

The advance care planning process starts with an open and honest discussion with your care team about your prognosis—what you may experience in the coming months—and the medications or therapies that may give you the best quality of life. Quality of life refers to a person's overall enjoyment of life, including their sense of well-being and ability to participate in their usual activities. This discussion should include important people in your life such as your spouse or partner and family members or friends who are likely to be with you at the end.

Make your wishes clear. It's important that everyone clearly understands the goals of your care and your personal wishes about what should—and should not—be done. You can decide if there is a point where you might want to stop cancer treatment. You can also decide what treatments you would want for symptom relief.

Once you've made these decisions, you'll fill out a legal document that explains what you want to be done if you aren't able to tell your care team yourself. This document is called an advance directive. Your health care providers are required to follow the instructions in an advance directive when you're too ill to make decisions about your care.

Tell your care team and family about your advance directive and its contents. Give a copy of your advance directive to all your doctors. Make sure you give a copy to anyone you've authorized to make decisions on your behalf (health care proxy). If your family or loved ones disagree with your plan, speak to your care team. Sometimes they or other specialists can help you and your family navigate these difficult conversations.

You can change your advance care plan at any time. Frequent conversations with your care team can help.

End-of-life considerations

End-of-life care provides medical, psychological, and spiritual support for people who are close to the end of life as well as the people who love them. The goal is comfort, not a cure. It may also be called comfort care or hospice. Note that hospice is a special kind of end-of-life care. Hospice refers specifically to an insurance benefit for people whose life expectancy is 6 months or less. Hospice supports those at the end of life by bringing in additional care providers and resources such as home care.

The goal of end-of-life care is to give people the best life possible with the time they have left. Care can be provided in your home, a hospice facility, or even in the hospital. A major goal is to keep you pain-free and make sure that you can leave this world comfortably and with dignity. Hospice doctors, nurses, social workers, and chaplains are experts in helping patients work through the spiritual and emotional challenges of coping with the end of life.

Providing support for family members is a key part of hospice care. Most programs offer counseling and support groups for family members, including support after the patient has died. This is referred to as bereavement. It can be very comforting to know that your loved ones will have that kind of support after you're gone.

Key points

- Supportive care is for relieving symptoms and side effects, and for other health issues related to cancer.
- You can also get support for psychological, social, and spiritual issues.
- Supportive care is given at any stage of disease, not just at the end of life.
- Supportive care is treatment that involves the whole person, not just their cancer.
- Many people with prostate cancer experience anxiety and depression. Help is available.
- A support group provides the opportunity to talk with others who've been through similar experiences.
- For help with financial support and transportation options, talk with your care team's social worker, patient navigator, and hospital financial services staff.
- Survivorship focuses on the health and well-being of a person with cancer from diagnosis until the end of life.

- Quality of life refers to a person's overall enjoyment of life, including their sense of well-being and ability to participate in regular activities.
- Advance care planning is done to ensure that your end-of-life wishes are understood and respected.
- An advance directive is a legal document that explains your care if you're too ill to give instructions yourself.
- Hospice care is for people who are close to the end of life. It's focused on comfort and quality of life.
- A key part of hospice care is providing support to family members.

7 Making treatment decisions

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

It's your choice

Treatment decisions are very personal. What's important to you may not be important to someone else. In shared decision-making, you and your care team share information, discuss the options, and agree on a treatment plan. Be clear about your goals for treatment and find out what to expect from treatment. It starts with an open and honest conversation between you and your team.

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

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments like hormone therapy or radiation
- > Your feelings about pain or side effects
- Cost of treatment, travel to treatment centers, and time away from school or work

- > Quality of life and length of life
- How active you are and the activities that are important to you

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

Second opinion

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

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

Things you can do to prepare:

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



Things to think about when making treatment decisions

Be sure to weigh all your options. There are no "correct" answers. The right decision is the one that's best for you. Consider:

Your personal preferences	VS.	Your health care providers' recommendations
Having definitive treatment	VS.	Keeping other treatment options open
Length of life	VS.	Quality of life
Traveling for treatment	VS.	Staying close to home and family
Having more treatment	VS.	Having more side effects
Having standard treatment now, which is covered by your health plan	VS.	Waiting for specialized treatment, which requires your health plan's approval

Questions to ask

Possible questions to ask your care providers are listed on the following pages. Feel free to use these or come up with your own. Have a notebook handy to jot down the answers to your questions.

Questions about cancer testing

- 1. What tests will I have?
- 2. Do the tests have any risks?
- 3. Will my health plan pay for all the tests you're recommending?
- 4. Do I need to do anything to prepare for testing?
- 5. Should I bring someone with me to the appointments?
- 6. Where do I go for testing, and how long will it take?
- 7. If any of the tests will hurt, what will you do to make me comfortable?
- 8. How soon will I know the results and who will explain them to me?
- 9. How can I get a copy of the pathology report and other test results?
- 10. What is the cancer stage? What does this stage mean in terms of survival?

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Questions about treatment choices

- 1. What are my treatment options?
- 2. Are you suggesting options other than what NCCN recommends? If yes, why?
- 3. What will happen if I do nothing?
- 4. Does any option offer a cure or long-term cancer control?
- 5. How do my age, sex, overall health, and other factors affect my options?
- 6. Will the treatment hurt?
- 7. How long do I have to decide about treatment? Is there a social worker or someone who can help me decide?
- 8. Is a clinical trial an option for me?
- 9. How do I get a second opinion?

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Questions about treatment outcomes

- 1. Does this hospital or cancer center offer the best treatment for me?
- 2. Do I have a choice of when to begin treatment?
- 3. How long will treatment last?
- 4. How will you know if treatment is working?
- 5. What are the chances of the cancer worsening or returning?
- 6. What follow-up care is needed after treatment?
- 7. Who should I contact with questions or concerns if the office is closed?

Questions about side effects

- 1. What are the possible complications and side effects of treatment?
- 2. Which side effects are most common and how long do they usually last?
- 3. Which side effects are serious or life-threatening?
- 4. Are there any long-term or permanent side effects?
- 5. What symptoms should I report right away? Who do I contact?
- 6. Will treatment affect my ability to urinate? Or have an erection?
- 7. What can I do to prevent or relieve the side effects of treatment?
- 8. Do any medications worsen side effects?
- 9. Do any side effects lessen or worsen in severity over time?
- 10. Will you stop or change treatment if there are serious side effects?

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Questions about your care team's experience

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

Questions about clinical trials

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

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Questions about resources and support

- 1. Will my health plan cover the treatment you're recommending?
- 2. How much will I have to pay for my treatment?
- 3. What help is available to pay for medicines and other treatments?
- 4. Is assistance available for transportation, childcare, and home care?
- 5. Who can I talk to about help with housing, food, and other needs?
- 6. Who can help me with my concerns about missing work or school?
- 7. What other supportive care services are available to me and my caregivers?
- 8. How can I find in-person or online support?
- 9. Who can I talk to if I don't feel safe at home, at work, or in my neighborhood?

Resources

Cancer Hope Network Cancerhopenetwork.org

FORCE: Facing Our Risk of Cancer Empowered facingourrisk.org

Malecare malecare.org

MSI Insiders msiinsiders.org

National Alliance of State Prostate Cancer Coalitions (NASPCC) naspcc.org

PCaAware National Prostate Cancer Awareness Foundation pcaaware.org

Prostate Conditions Education Council (PCEC) prostateconditions.org

Prostate Health Education Network (PHEN) prostatehealthed.org Triage Cancer triagecancer.org

Veterans Prostate Cancer Awareness Inc. <u>vpca.vet</u>

ZERO Prostate Cancer zerocancer.org



Take our survey, and help make the NCCN Guidelines for Patients better for everyone!

NCCN.org/patients/comments



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Words to know

advanced-stage prostate cancer

Prostate cancer that has spread beyond the prostate to other areas in the body. This includes regional and metastatic prostate cancer.

androgen deprivation therapy (ADT)

Hormone therapy that stops the body from making testosterone or blocks cancer cells from using testosterone. ADT can be given

anti-androgen

A drug that stops the action of the hormone testosterone.

biopsy

A procedure that removes fluid or tissue

castration

Surgery that removes the testicles, or drugs that suppress the function of the testicles, to minimize testosterone levels.

computed tomography (CT)

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

digital rectal exam

An exam of the prostate by feeling it through the wall of the rectum.

early-stage prostate cancer

Prostate cancer that stays within the prostate and usually grows slowly.

enlarged prostate

An overgrowth of tissue in the prostate that isn't caused by cancer. Also called benign prostatic hyperplasia.

through drugs or surgery.

samples to be tested for disease.

life expectancy The number of years a person is likely to live based on statistics of other people in similar

circumstances.

erectile dysfunction

getting or staying erect.

genetic abnormality

hormone therapy

deprivation therapy.

the body.

mutation.

A lack of blood flow to the penis that limits

external beam radiation therapy (EBRT)

A treatment in which a machine outside the body aims radiation precisely at cancer inside

An abnormal change in the cell's instructions

for making and controlling cells. Also called a

A cancer treatment that stops the making or action of hormones. Also called androgen

luteinizing hormone-releasing hormone (LHRH) agonist

A drug that acts in the brain to stop the testicles from making testosterone.

luteinizing hormone-releasing hormone (LHRH) antagonist

A drug that acts in the brain to stop the testicles from making testosterone.

lymphatic system

A network of organs and vessels that fights infections and transports a fluid called lymph.

lymph nodes

Small clusters found throughout the body that filter lymph fluid to remove germs.

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magnetic resonance imaging (MRI)

A test that uses radio waves and powerful magnets to make pictures of the insides of the body.

metastasis

The spread of cancer from the site where it started to a new site in the body.

metastatic prostate cancer

Cancer that spreads beyond the prostate to other parts of the body.

nomogram

A mathematical tool that uses health information to predict an outcome.

observation

A period of watching for cancer occurrence or growth while not receiving treatment.

orchiectomy

An operation to reduce testosterone in the body by removing one or both testicles.

palliative therapy

Health care for the symptoms of cancer or the side effects of cancer treatment. Palliative therapy is an important part of supportive care.

pathologist

A doctor who specializes in testing cells and tissue to find disease.

pelvic lymph node dissection (PLND)

An operation that removes lymph nodes in the pelvis (between the hip bones).

perineum

The body region between the scrotum and anus.

positron emission tomography (PET)

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

prostate-specific antigen (PSA)

A protein made by the prostate that helps semen transport sperm. PSA is measured in nanograms per milliliter of blood (ng/mL).

prostate-specific membrane antigen (PSMA)

A protein found on the surface of prostate cancer cells. PSMA is a biomarker of prostate cancer cells.

PSA persistence

When PSA level is still detectable after prostate cancer treatment.

PSA recurrence

When PSA level drops after prostate cancer treatment but then rises again.

radiation therapy

Treatment that uses high-energy rays (radiation) to kill cancer cells and stop new cancer cells from being made.

radical prostatectomy

An operation that removes the entire prostate as well as surrounding tissue, seminal vesicles, and sometimes nearby lymph nodes.

recurrence

The return of cancer after a disease-free period.

regional prostate cancer

Cancer that has grown from the prostate to neighboring areas, but no farther.

risk factor

Something that increases the chance of getting a disease.

seminal vesicles

Glands that make and store part of the fluid that becomes semen.

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Prostate Cancer, Version 4.2023. It was adapted, reviewed, and published with help from the following people:

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NCCN Cancer Centers

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

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

City of Hope National Medical Center Duarte, California 800.826.4673 • <u>cityofhope.org</u>

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

Duke Cancer Institute Durham, North Carolina 888.275.3853 • <u>dukecancerinstitute.org</u>

Fox Chase Cancer Center Philadelphia, Pennsylvania 888.369.2427 • <u>foxchase.org</u>

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

Fred Hutchinson Cancer Center Seattle, Washington 206.667.5000 • <u>fredhutch.org</u>

Huntsman Cancer Institute at the University of Utah Salt Lake City, Utah 800.824.2073 • healthcare.utah.edu/huntsmancancerinstitute

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

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

NCCN Guidelines for Patients® Advanced-Stage Prostate Cancer, 2023 Memorial Sloan Kettering Cancer Center New York, New York 800.525.2225 • mskcc.org

Moffitt Cancer Center Tampa, Florida 888.663.3488 • <u>moffitt.org</u>

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

Robert H. Lurie Comprehensive Cancer Center of Northwestern University *Chicago, Illinois* 866.587.4322 • <u>cancer.northwestern.edu</u>

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 • <u>siteman.wustl.edu</u>

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

Stanford Cancer Institute Stanford, California 877.668.7535 • <u>cancer.stanford.edu</u>

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

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

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

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

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

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

UCLA Jonsson Comprehensive Cancer Center Los Angeles, California 310.825.5268 • <u>cancer.ucla.edu</u>

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

University of Colorado Cancer Center Aurora, Colorado 720.848.0300 • <u>coloradocancercenter.org</u>

University of Michigan Rogel Cancer Center Ann Arbor, Michigan 800.865.1125 • <u>rogelcancercenter.org</u>

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

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

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

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



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Take our survey to let us know what we got right and what we could do better.

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