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## Patient education: Treatment for advanced prostate cancer (Beyond the Basics)

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### INTRODUCTION

Prostate cancer is a cancer of the prostate gland, an organ that forms a ring around the urethra near its connection to the bladder ( [figure 1](#)). The urethra is the tube that carries urine from the bladder to the outside of the body.

Prostate cancer is advanced if it has spread beyond the prostate gland and the area around the prostate. Some men with newly diagnosed prostate cancer have advanced prostate cancer (see ['Prostate cancer staging'](#) below). In other men, advanced prostate cancer will develop after they are originally treated for localized disease.

Advanced prostate cancer is usually treated with a combination of different approaches, which may include hormone therapy, chemotherapy, immunotherapy, or radiation. Some men may be offered surgery to remove the prostate if their cancer's spread appears to be limited to the lymph nodes and there is no evidence of spread to other parts of the body. In other cases, such as when the cancer has spread to the bones or other tissues in the body (called "distant metastasis"), surgery is not typically offered. Although metastatic prostate cancer is not curable, treatment can often help to

control the cancer for prolonged periods of time. This can help to reduce symptoms and improve the quality of life.

This article will discuss the treatment of men with advanced prostate cancer. A separate article discusses the treatment of earlier stage (stage I to III), localized prostate cancer. (See ["Patient education: Prostate cancer treatment; stage I to III cancer \(Beyond the Basics\)"](#).)

More detailed information about prostate cancer, written for health care providers, is available by subscription. (See ["Professional level information"](#) below.)

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## CANCER CARE DURING THE COVID-19 PANDEMIC

COVID-19 stands for "coronavirus disease 2019." It is an infection caused by a virus called SARS-CoV-2. The virus first appeared in late 2019 and has since spread throughout the world. People in many areas have been told to stay home as much as possible in order to slow the spread of the virus. This is particularly important for people with cancer, as many of them are at increased risk of severe illness if they get COVID-19. However, this risk must be balanced against the importance of continuing to get regular medical care to monitor and treat their cancer.

If you are undergoing treatment for cancer, your oncologist can talk to you about whether you should make any changes to your usual regimen or schedule. In some cases, it may be an option to reduce the number of appointments you need to attend in person. This will depend on several different things, including where you live, the type and stage of your cancer, the available treatment options, and your overall health.

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## PROSTATE CANCER STAGING

Staging is a system used to describe the size, aggressiveness, and spread of a cancer. A cancer's stage helps to guide treatment and can help predict the chance of curing the cancer.

Stage IV prostate cancer (also called metastatic prostate cancer) has spread outside of the prostate ([figure 1](#)). Stage IV cancer can mean that there is spread locally to involve the bladder or rectum, spread to the lymph nodes, or spread to other more distant areas, like the bones. As mentioned above, a subset of men with stage IV cancer might be offered surgery to remove the prostate, although this is typically not an option for men whose cancer has spread beyond the prostate and lymph nodes.

Men who have been treated for stage I, II, or III ("localized") prostate cancer are monitored with regular blood tests to check their prostate-specific antigen (PSA) level. If the PSA level rises after

local treatment, it indicates that the tumor may have recurred in the area of the prostate or spread to distant sites. The decision on how to treat a man with a rising PSA is based on several different factors, including which treatments he has already had (and how the cancer responded), how quickly the PSA level is rising, and the likelihood that the cancer has spread to parts of the body other than the prostate. (See "[Patient education: Prostate cancer treatment; stage I to III cancer \(Beyond the Basics\)](#)", [section on 'Monitoring for a recurrence of the tumor'](#).)

The following sections will describe the various treatment options for distant metastases from prostate cancer.

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## STAGE IV (METASTATIC) PROSTATE CANCER TREATMENT

**When to start treatment** — Different doctors have different approaches for when to start treatment for advanced prostate cancer:

- Many doctors recommend starting treatment that lowers the body's testosterone level with drugs (termed "androgen deprivation therapy" [ADT]) when advanced prostate cancer is first diagnosed (even if metastases have not yet been identified); the hope is that treatment will slow the growth of the cancer and possibly prolong survival.
- Others believe that early treatment is not curative and can cause bothersome side effects. Doctors who feel this way may recommend delaying the start of treatment until metastases are evident or until symptoms of cancer (like bone pain) develop.

Since everyone's situation is different, it's important to discuss the benefits and risks of each approach with your doctor in order to decide which approach is best for you.

### Options for initial treatment

**Androgen deprivation therapy** — Male hormones (androgens, the most common of which is testosterone) fuel the growth of prostate cancer. Treatments that decrease the body's levels of androgens can also decrease the size of the cancer in the prostate as well as other areas (metastases). These treatments are called "androgen deprivation therapy" or "ADT."

ADT is usually recommended as the initial treatment for men with metastatic prostate cancer. ADT may be combined with another drug, either [abiraterone](#) or a chemotherapy agent called [docetaxel](#) (see '[Abiraterone](#)' below and '[Chemotherapy](#)' below). The recommended treatment approach depends on several factors, including how quickly the disease is expected to progress and the number and location of metastases.

ADT can be done by taking medicines that interfere with androgens or by having surgery to remove the testicles (called an "orchiectomy," also known as castration). In many countries, including the United States, the use of medicines is usually preferred over surgery. The medicines used in this context have the same effect as surgery, as they are a form of "chemical castration" (meaning that they stop the production of androgens even though the testicles are not removed).

Examples of the medicines used for ADT include the following:

- **GnRH agonists** – Gonadotropin-releasing hormone (GnRH) agonists are medicines that temporarily "turn off" the testicles' production of male hormones (androgens). This starves the cancer cells, causing the prostate to shrink. GnRH agonists are given as a shot every one to six months or as a depot that lasts 12 months, and they include [leuprolide](#) (sample brand name: Lupron) and [goserelin](#) (brand name: Zoladex). Sometimes, at the beginning of treatment, there may be a temporary surge in the body's levels of androgens before they begin to decline (called a "flare"). Some men may experience a worsening of symptoms (eg, bone pain) because of a temporary growth of the tumor during this brief period. One way doctors can try to avoid this is to add a second medicine, called an "antiandrogen," to the GnRH agonist, at least initially (see below).
- **GnRH antagonist** – [Degarelix](#) (brand name: Firmagon) is a GnRH antagonist that temporarily "turns off" the testicles' production of male hormones (androgens). This medicine is more rapidly acting than a GnRH agonist and may be useful for situations where there is major concern about the disease temporarily progressing before treatment becomes effective.
- **Combined androgen blockade** – Some doctors recommend a second medicine, called an "antiandrogen," in addition to the GnRH agonist. Examples of antiandrogens include [flutamide](#) (sample brand name: Eulexin) and [bicalutamide](#) (brand name: Casodex). These medicines are especially helpful when GnRH agonists are being started. That's because GnRH agonists actually boost androgen production for a short time at the beginning, before they shut down its production. This boost can temporarily cause the cancer to flare (get worse). The antiandrogen blocks that flare.

Men taking a GnRH agonist or a GnRH antagonist generally take these medicines continuously. Although some doctors have suggested taking breaks by being off treatment for a little while and then restarting the treatment ("intermittent ADT"), this approach has not been shown to be as effective as continuous ADT.

As mentioned, in many places, medication is preferred over surgery for ADT. However, in some countries, surgical castration is performed more frequently. There are also some situations in which surgery is done in order to decrease the testosterone level immediately, rather than waiting for

medications to take effect. Some men may also choose to have surgery rather than take medication regularly for cost or convenience reasons. Men who do have surgery can get artificial (prosthetic) testicles implanted in order to preserve a normal appearance.

**Side effects of ADT** — The side effects of ADT are related to the lowered levels of male hormones and include the following:

- Decreased libido (sex drive) and difficulties with erection (erectile dysfunction)
- Hot flashes
- Enlargement of the breasts (called gynecomastia) (see "[Patient education: Gynecomastia \(breast enlargement in men\) \(Beyond the Basics\)](#)")
- Loss of muscle and an increase in body fat
- Thinning and weakening of the bones (called "osteoporosis"), which can increase the risk of bone fractures (see "[Patient education: Osteoporosis prevention and treatment \(Beyond the Basics\)](#)")
- An increased risk of developing type 2 diabetes
- A potential small increased risk of developing or worsening coronary heart disease, which can lead to heart attack (although this is controversial)

Many of these side effects are serious, and they might seem frightening. However, not all men have these side effects. In addition, it is important to balance the risk of side effects with the risk of not using ADT, which could allow your cancer to grow or spread. In most men, the risk of the cancer growing or spreading outweighs the possible risk of side effects. In addition, there are ways to prevent or treat many of these side effects.

**Abiraterone** — [Abiraterone](#) (brand name: Zytiga) is a medication that blocks the production of androgens by the prostate cancer itself, as well as in the testes and adrenal glands. It is often given in combination with ADT, as combined therapy can improve survival (how long a man will live) over ADT alone.

[Abiraterone](#) has been shown to improve survival in men with advanced prostate cancer whether or not they have already been treated with chemotherapy. Abiraterone must be taken with a steroid to avoid a serious complication. Abiraterone's side effects can include fluid retention and a drop in blood potassium levels.

**Enzalutamide, apalutamide, and darolutamide** — [Enzalutamide](#) (brand name: Xtandi), [apalutamide](#) (brand name: Erleada), and [darolutamide](#) (brand name: Nubeqa) are other, newer agents that block the effects of androgens in stimulating the growth of the prostate cancer cells.

[Enzalutamide](#) has been shown to increase survival in men with metastatic prostate cancer who are no longer responding to hormone therapy alone (known as "castration-resistant" prostate cancer) and who have already been treated with chemotherapy.

In addition, all three drugs ([enzalutamide](#), [apalutamide](#), and [darolutamide](#)) have been shown to increase survival in men with nonmetastatic castration-resistant prostate cancer who have not yet received chemotherapy, delaying both the progression of the disease and the need for chemotherapy in this setting.

Finally, the addition of either [enzalutamide](#) or [apalutamide](#) to ADT has led to improved outcomes compared with ADT alone in men with newly diagnosed metastatic prostate cancer who have not yet been treated with ADT ("castration-sensitive" prostate cancer). (See '[Androgen deprivation therapy](#)' above.)

**Chemotherapy** — Chemotherapy is a treatment given to slow or stop the growth of cancer cells. In the past, chemotherapy was reserved for men whose advanced prostate cancer was no longer responding to ADT (castration-resistant prostate cancer). Chemotherapy is now often recommended in combination with ADT as the initial treatment for men whose cancer has already spread outside of the prostate, typically to the bones or other organs. Chemotherapy given when treatment is first started may improve survival over ADT alone.

The most commonly used chemotherapy agents are [docetaxel](#) (brand names: Docefrez, Taxotere) and [cabazitaxel](#) (brand name: Jevtana). Most of the drugs are given into the vein (intravenously [IV]).

Chemotherapy is not given every day, but instead, it is given in cycles. A cycle of chemotherapy (which is typically 21 days) refers to the time it takes to give the treatment and then allow the body to recover from the side effects of the medicines.

Side effects of chemotherapy can include the following:

- Temporary hair loss
- Nausea and vomiting
- A decrease in the number of blood cells that fight infection (white blood cells), which increases the risk of developing an infection

**Options at the time of disease progression** — Most men with advanced prostate cancer initially respond well to treatment that includes ADT (which is often given in combination with [docetaxel](#)), but then their prostate cancer comes back, often within a few years. At this point, the cancer may be termed "castration resistant" or "castrate resistant," meaning that ADT is no longer effective. When this occurs, your doctor will work with you to choose another ("secondary") form of treatment to try.

**Secondary hormone therapy** — Even when prostate cancer becomes castration resistant, some form of ADT is continued because at least a portion of the cancer cells might still respond. (See ['Androgen deprivation therapy'](#) above.)

Secondary hormone therapy can include the following:

- Adding an antiandrogen (such as [bicalutamide](#), [nilutamide](#), or [flutamide](#)) in men who have thus far been treated only with GnRH agonists.
- Stopping the antiandrogen in men who were treated with combined androgen blockade.
- Trying a different type of antiandrogen (eg, [enzalutamide](#) or [apalutamide](#)). Cancer that is resistant to one antiandrogen treatment may not be resistant to another.
- Trying another medicine that blocks the activity of androgen in the body, including estrogen, steroids, or the antifungal medication [ketoconazole](#).
- [Abiraterone](#), which blocks androgens from being made in the tumor and in the rest of the body.

**Chemotherapy** — Chemotherapy may be offered to men with advanced prostate cancer who have stopped responding to their initial therapy, including all forms of hormone therapy. (See ['Chemotherapy'](#) above.)

**Immunotherapy** — A newer approach to treating advanced prostate cancer involves immunotherapy. This is a type of treatment that uses the body's immune system to help slow or stop cancer growth.

**Cancer vaccine** — One form of immunotherapy involves the use of a cancer vaccine called "[sipuleucel-T](#)" (brand name: Provenge). This vaccine is made by isolating white blood cells (dendritic cells) from the patient's blood and stimulating them outside of the body with various chemicals to build the body's immunity against the cancer. These cells are then reinjected into the patient three times at intervals of two weeks.

Side effects with this cancer vaccine have generally been mild and include chills, fever, fatigue, nausea, and headache.

**Checkpoint inhibitor immunotherapy** — Another immunotherapy approach is use of a group of medications called "checkpoint inhibitors." "Checkpoints" are a built-in part of the immune system intended to prevent it from attacking healthy cells. Checkpoint inhibitors act on certain checkpoints in order to identify and destroy cancer cells. Several checkpoint inhibitors are used to treat other types of cancer; these work by stimulating cells called "T cells" in order to attack the cancer. These medications are not yet approved for use in people with prostate cancer, but they are being studied.

**Men with bone metastases** — The bones are a common place for prostate cancer to spread. ADT can often control the cancer that has spread to the bones.

Men whose metastases are mostly in their bones may also be treated with radium-223. (See ['Radium-223'](#) below.)

Men who develop bone pain in one or a few bones as a result of the cancer can be treated with radiation therapy to relieve their pain. The radiation is usually given in one or a few visits, similar to having an X-ray. Some people have worsened pain for one to two days immediately after the radiation treatment. However, most people feel partial or complete improvement of pain within a week after treatment.

Men with bone metastases can also benefit from medicines called "osteoclast inhibitors," such as [denosumab](#) (brand name: Xgeva) or [zoledronic acid](#) (brand name: Zometa). These medicines can help prevent fractures, the need for bone surgery, spinal cord compression, and the need for radiation therapy to treat pain.

**Radium-223** — [Radium-223](#) is a radioactive element that localizes in bone. For men whose advanced prostate cancer consists almost exclusively of extensive bone metastases, treatment with radium-223 is often effective at relieving bone pain, preventing complications (broken bones, need for radiation therapy, spinal cord injury caused by the cancer), and extending life. While radium-223 is usually combined with ADT, it has not been studied in combination with other therapies, such as chemotherapy or [abiraterone](#), and it is not recommended in combination with these agents.

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## CLINICAL TRIALS

Progress in treating cancer requires that better treatments be identified through clinical trials, which are conducted all over the world. A clinical trial is a carefully controlled way to study the effectiveness of new treatments or new combinations of known therapies. Ask for more information about clinical trials or read about clinical trials at:

- [www.cancer.gov/clinicaltrials/](http://www.cancer.gov/clinicaltrials/)
- <http://clinicaltrials.gov/>

Videos addressing common questions about clinical trials are available from the American Society of Clinical Oncology (<http://www.cancer.net/pre-act>).

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## WHERE TO GET MORE INFORMATION



Your health care provider is the best source of information for questions and concerns related to your medical problem.

This article will be updated as needed on our website ([www.uptodate.com/patients](http://www.uptodate.com/patients)). Related topics for patients, as well as selected articles written for health care professionals, are also available. Some of the most relevant are listed below.

**Patient level information** — UpToDate offers two types of patient education materials.

**The Basics** — The Basics patient education pieces answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials.

[Patient education: Prostate cancer \(The Basics\)](#)

**Beyond the Basics** — Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are best for patients who want in-depth information and are comfortable with some medical jargon.

[Patient education: Prostate cancer treatment; stage I to III cancer \(Beyond the Basics\)](#)

[Patient education: Gynecomastia \(breast enlargement in men\) \(Beyond the Basics\)](#)

[Patient education: Osteoporosis prevention and treatment \(Beyond the Basics\)](#)

**Professional level information** — Professional level articles are designed to keep doctors and other health professionals up-to-date on the latest medical findings. These articles are thorough, long, and complex, and they contain multiple references to the research on which they are based. Professional level articles are best for people who are comfortable with a lot of medical terminology and who want to read the same materials their doctors are reading.

[Initial systemic therapy for castration-sensitive prostate cancer](#)

[Side effects of androgen deprivation therapy](#)

[Overview of the treatment of disseminated castration-sensitive prostate cancer](#)

[Bone metastases in advanced prostate cancer: Management](#)

[Castration-resistant prostate cancer: Treatments targeting the androgen pathway](#)

[Chemotherapy in advanced castration-resistant prostate cancer](#)

[Immunotherapy for castration-resistant prostate cancer](#)

[Alternative endocrine therapies for castration-resistant prostate cancer](#)

[Bone metastases in advanced prostate cancer: Clinical manifestations and diagnosis](#)

[Prostate cancer: Risk stratification and choice of initial treatment](#)

[Rising serum PSA after treatment for localized prostate cancer: Systemic therapy](#)

The following organizations also provide reliable health information:

- National Cancer Institute

1-800-4-CANCER

([www.cancer.gov/cancertopics/types/prostate](http://www.cancer.gov/cancertopics/types/prostate))

- National Library of Medicine

([www.nlm.nih.gov/medlineplus/prostatecancer.html](http://www.nlm.nih.gov/medlineplus/prostatecancer.html))

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