Advanced Prostate Cancer Treatment

WHAT IS ADVANCED PROSTATE CANCER?

Prostate cancer is often grouped into four stages.

- **Stages I & II**: The tumor hasn’t spread beyond the prostate. This is often called “early stage” or “localized” prostate cancer.
- **Stage III**: Cancer has spread outside the prostate, but only to nearby tissues. This is often called “locally advanced prostate cancer.”
- **Stage IV**: Cancer has spread outside the prostate to other parts such as the lymph nodes, bones, liver or lungs. This stage is often called “advanced prostate cancer.”

When an early stage prostate cancer is found, it may be treated or left alone. If prostate cancer spreads beyond the prostate or returns after treatment, it’s often called advanced prostate cancer.

Stage IV prostate cancer is not “curable,” but there are many ways to control it. Treatment can stop advanced prostate cancer from growing and causing symptoms and help you feel better, longer. It helps to talk about your treatment options with a skilled healthcare provider.

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TYPES OF ADVANCED PROSTATE CANCER

- **Biochemical Recurrence**: Prostate Specific Antigen (PSA) level has risen after the first treatment(s) with no other sign of cancer.
- **Non-Metastatic Castration-Resistant Prostate Cancer (nmCRPC)**: Prostate cancer growth is found even after the hormone (testosterone) is blocked in patients who have had biochemical failure. This is found by a rise in the PSA level, while the testosterone level stays low. Imaging tests do not show signs the cancer has spread.
- **Metastatic Prostate Cancer**: Cancer cells have spread beyond the prostate. Cancer spread may be seen on imaging studies. Imaging tests may show that the cancer has spread.
- **Metastatic Castration-Resistant Prostate Cancer (mCRPC)**: Metastatic prostate cancer has been treated with androgen ablation therapy lowering testosterone levels; but, PSA levels keep rising and/or metastatic spots are growing.

SIGNS OF ADVANCED PROSTATE CANCER

Men with advanced prostate cancer may or may not have symptoms. Symptoms depend on the size of new growth and where the cancer has spread in the body. With advanced disease, mainly if you have not had treatment to the prostate itself, you may have problems passing urine or see blood in your urine. Some men may feel tired, weak or lose weight. When prostate cancer spreads to bones, you may have bony pain. Tell your doctor and nurse about any pain or other symptoms you feel. There are treatments that can help.
HOW IS ADVANCED PROSTATE CANCER TREATED?

The goal of advanced prostate cancer treatment is to shrink the tumor(s), control symptoms and help you to live longer. For biochemical recurrence, nmCRPC, metastatic prostate cancer, and/or mCRPC there could be a lot of treatment choices to talk about. It is best to talk to your doctor about how to handle side effects before you choose a plan. Which treatment to use, and when, will depend on discussions with your doctor.

Treatment options include:

Hormone Therapy or Androgen Deprivation Therapy (ADT)

Testosterone is the main hormone that fuels the growth of prostate cancer cells. Stopping or blocking testosterone can slow cancer growth. This can be done by taking prescribed drugs or having an operation to remove the testicles that make the hormone. These treatments are called hormone therapy, or Androgen Deprivation Therapy (ADT) because they lower androgen (male sex hormone) levels or blocks its effects. There are many side effects to keep in mind. Types of hormone therapy are:

- **Orchiectomy (surgery to remove the testicles).** This surgery removes the testicles to stop the body from making testosterone. It is a simple surgery where the patient can go home the same day. It is rarely used as a treatment choice in the United States.

- **LHRH or GnRH agonists (analogs).** These are drugs that lower testosterone levels. Some types are: Leuprolrelin (Lupron Depot®) and (Eligard®), Goserelin (Zoladex®), Triptorelin (Trelstar®), and Histrelin (Vantas®). They are given as shots or as small pellets placed under the skin. Based on the drug used, they are given from once/month to once/6 months.

- **LHRH or GnRH antagonists.** These are drugs that also lower testosterone, but more quickly. Degarelix (Firmagon®) is an LHRH antagonist given as a monthly shot under the skin for advanced prostate cancer.

- **Anti-androgen drugs.** These drugs block testosterone from linking to the cancer cells. Drugs such as Flutamide (Eulexin®), Bicalutamide (Casodex®), and Nilutamide (Nilandvon®) are given as a daily pill.

- **CAB (combined androgen reducing treatment, with anti-androgens).** This method blends castration (by surgery or with the drugs described above) and anti-androgen drugs. The treatment blocks testosterone and stops it from binding to cancer cells.

- **Androgen synthesis inhibitors.** These drugs stop other parts of your body (and the cancer itself) from making more testosterone and its metabolites. Abiraterone acetate (Zytiga®) is a drug you take as a pill and is taken with another pill, Prednisone. It may be used before or after chemotherapy in men with mCRPC. These drugs are often called second-generation anti-androgen and are used along with other antiandrogen therapies.

- **Androgen receptor binding inhibitors.** These drugs block testosterone from linking to prostate cancer cells (like anti-androgens). Enzalutamide (Xtandi®) is taken as a pill. You do not need to take a steroid with this drug. It may be used before or after chemotherapy in men with mCRPC. Enzalutamide is also thought of as a second-generation anti-androgen and, like abiraterone, is used along with other antiandrogen therapies.

There are many benefits and risks to each type of hormone therapy so be sure to ask questions to your doctor so you understand what is best for you.

Chemotherapy

Chemotherapy drugs can slow the growth of cancer. It can reduce symptoms and extend life. The main chemotherapy drugs Docetaxel (Taxotere®) and Cabazitaxel (Jevtana®) have been shown to help.

Immunotherapy

Immunotherapy uses the body's immune system to fight cancer. It is a choice for men with mCRPC who have no symptoms or only a few. If the cancer returns and spreads, your doctor may offer Sipuleucel-T (Provenge®). This is a cancer vaccine that can boost your immune system so that it can attack the cancer cells.

Oral Drug Treatments

There are two new drug treatments taken by mouth to treat nmCRPC. Some men have done very well with these options, combined with ADT drugs. Apalutamide and Enzalutamide are used to stop the effects of androgens in the prostate and throughout the body to stop cancer growth. These drugs may slow down the spread of cancer.
There are also many drug combinations for patients with mCRPC. Your doctor may suggest some of the options below based on your symptoms:

• **Minor or no symptoms.** Options include Abiraterone + Prednisone, Enzalutamide, Docetaxel, or Sipuleucel-T may be offered.

• **Cancer that’s spread to bones.** Options include Abiraterone + Prednisone, Enzalutamide, Docetaxel, Radium-223.

• **Other treatments did not work well.** Options include Abiraterone + Prednisone, Enzalutamide, Ketoconazole + Steroid, Radionuclide Therapy.

• **Options for men who’ve taken Docetaxel.** Options include Abiraterone + Prednisone, Cabazitaxel or Enzalutamide, or often Radium-223 can help with bone pain.

**Bone-targeted Therapy**

Men with prostate cancer that has spread to the bones may get “skeletal-related events” (SREs). SREs include fractures, pain and other problems. Two drugs that can stop the cancer and reduce SRE’s are Zoledronic Acid (Zometa®) and Denosumab.

Radiopharmaceuticals are drugs with radioactivity. They can be used to help with bone pain from metastatic cancer. Some are called Strontium-89 (Metastron®) and Samarium-153 (Quadramet®). Radium-223 (Xofigo®) may also be used for men whose mCPRC has spread to their bones. It may be offered when ADT doesn’t work. It gives off small amounts of radiation that go to the exact parts where cancer cells are growing.

Calcium and/or Vitamin D are also used to help protect your bones. They are often urged for men on hormone therapy to treat prostate cancer.

**Radiation**

Radiation uses high-energy beams to kill tumors. It can help with pain and other symptoms if prostate cancer spreads to the bones.

For all treatments, it is of great value to ask your doctor about side effects and how to handle them.

**QUESTIONS TO ASK YOUR HEALTHCARE PROVIDER**

- Which treatment options do you suggest for me, and why?
- What are the pros/cons of each treatment?
- What side effects should I expect, and what should I do to handle side effects?
- Can you put me in touch with other patients who’ve received the treatment you suggest for me?
- Will my health plan cover the costs of treatment, or can you help me get financial aid?
- Will I need extra help from my spouse, partner or a friend during or after treatment?
- How can a clinical trial help me, and what trials should I keep in mind?
- What else can I do to stay healthy?

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To learn more, visit the Urology Care Foundation’s website, UrologyHealth.org/UrologicConditions or go to UrologyHealth.org/FindAUrologist to find a doctor near you.

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