



MANAGING ADVANCED PROSTATE CANCER



ZERO 
THE END OF PROSTATE **CANCER**



WHAT IS ADVANCED PROSTATE CANCER?

Whether you've been living with prostate cancer for years or are newly diagnosed, you have advanced prostate cancer if:

1. The prostate cancer cells have spread outside the capsule of the prostate gland to the tissue around the prostate, but not the lymph nodes (Stage III: localized advanced prostate cancer).
2. The prostate cancer cells have spread to the lymph nodes and/or organs and tissue distant from the prostate such as bones, liver, or lungs (Stage IV: metastatic prostate cancer).
3. Your prostate-specific antigen (PSA) level has risen at least three consecutive times after completion of primary treatment or while on androgen deprivation therapy or hormone reduction. At this point, the disease becomes castration-resistant.

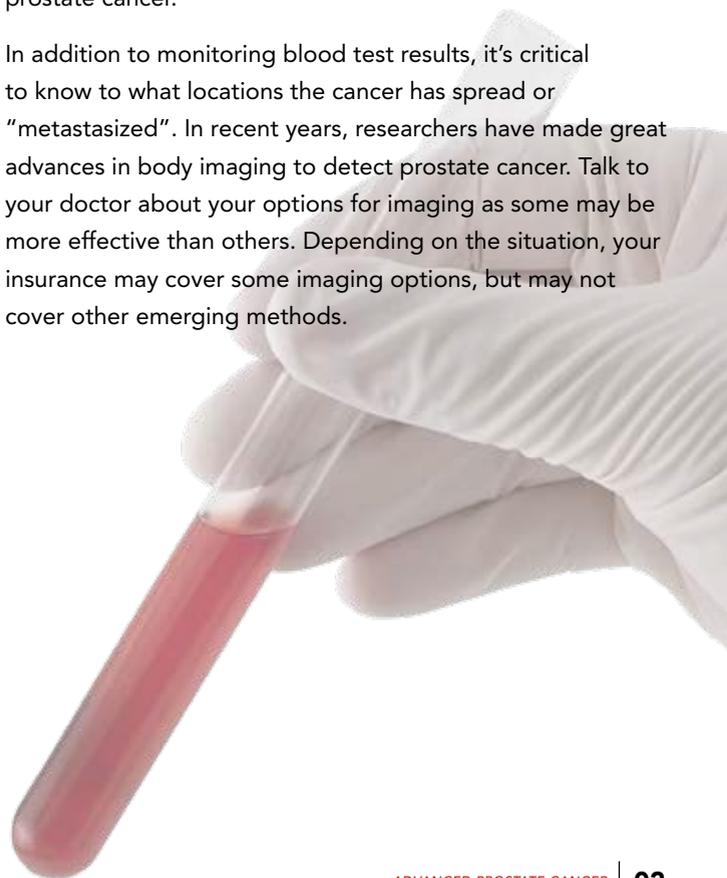
This brochure focuses primarily on Stage IV and castration-resistant prostate cancer.

DETERMINING YOUR DISEASE STATE

There is no cure for Stage IV prostate cancer. But there is hope, as many men are able to effectively manage the disease through treatments that were not available even ten years ago. Through these options, a patient is able to slow the progression and sometimes halt the growth of the cancer. Currently, doctors use the PSA and other tests to gauge the progression of advanced disease.

An important and typical sign of advanced disease is a rapid rise in PSA level over a short period of time following initial treatment, such as a radical prostatectomy or radiation therapy. Be sure to discuss this with your doctor, because there are other circumstances that may cause a temporary escalation in PSA levels. Your doctor should also evaluate your testosterone level, as testosterone acts as an accelerant to prostate cancer.

In addition to monitoring blood test results, it's critical to know to what locations the cancer has spread or "metastasized". In recent years, researchers have made great advances in body imaging to detect prostate cancer. Talk to your doctor about your options for imaging as some may be more effective than others. Depending on the situation, your insurance may cover some imaging options, but may not cover other emerging methods.



DETERMINING YOUR DISEASE STATE

	TYPICAL RESULT	STAGE
Initial Diagnosis	Rising PSA	Early Stage Stage I
Initial Treatment (surgery and/ or radiation)	Sharp drop in PSA (could drop to zero)	Early Stage Stage I
Treatment Failure	Gradual rise in PSA	Early Stage Stage II
Hormone Therapy (injections)	Drop in PSA	Early Stage Stage II
Treatment Failure	Sharp increase in PSA	Middle Stages Stage III
Secondary Hormone Therapy (emerging treatments, taken in addition to hormone shots, or clinical trials)	Moderate drop in PSA	Middle Stages Stage III
Treatment Failure	Sharp increase in PSA	Advanced Stage Stage IV
Treatment (radiation, immunotherapy, chemotherapy, or clinical trials)	Small to moderate drop in PSA	Advanced Stage Stage IV
Treatment Failure	Sharp increase in PSA	Advanced Stage Stage IV
Treatment (options not tried in previous steps or clinical trials)	Possible lowering of PSA levels	Advanced Stage Stage IV
Treatment Failure	Sharp increase in PSA	Advanced Stage Stage IV

ADVANCED PROSTATE CANCER

IDENTIFYING TREATMENT OPTIONS

HORMONE THERAPY

Hormone therapy, also called androgen deprivation therapy (ADT), is a prostate cancer treatment that alters the body's hormone balance to prevent cancer from growing. Hormone therapies can't kill prostate cancer, but they can improve quality of life and extend survival.

Hormone therapy is most often used when surgery is not an option, in conjunction with primary treatment if the cancer is labeled aggressive or "high risk", or if the cancer returns after initial treatment such as surgery or radiation therapy.

Orchiectomy, a procedure in which the testicles (which make 90 percent of the body's testosterone) are removed, is an option for men who prefer a one-time, low-cost procedure. However, the operation is permanent and irreversible.

There are several types of hormone therapies, including LHRH agonists, LHRH antagonists, anti-androgens, inhibitors, and blockers.

LHRH Agonists

Luteinizing hormone-releasing hormone (LHRH) is a key hormone released into the body prior to the production of testosterone. Blocking the release of LHRH with the use of LHRH therapies is the most common hormone therapy used on prostate cancer patients. Drugs in this class include Lupron®, Zoladex®, Trelstar®, and Eligard®. They are administered as regular shots in intervals ranging from once per month to once per year. LHRH agonists cause what is known as a "flare" reaction – a rise in testosterone during the first several weeks following a shot before the drug starts to take action.

IDENTIFYING TREATMENT OPTIONS

LHRH Antagonists

Antagonist medications are a newer class of drugs that can block LHRH from stimulating testosterone production without causing a testosterone flare (which can cause a temporary additional rise in PSA). This class includes Firmagon® and it's administered as a monthly shot.

Anti-Androgens

The testosterone flare associated with LHRH drugs can be prevented with anti-androgens such as flutamide, Casodex®, and Nilandron®. These drugs can help block the action of testosterone in prostate cancer cells and are almost always used in conjunction with LHRH agonists.

When taken alone, anti-androgens come with positives and negatives. They can cause fewer sexual side effects than LHRH agonists, but they are not as effective as an orchiectomy or LHRH agonists in treating the disease, making them a poor choice on their own for many men with metastatic prostate cancer.

These initial hormone therapies are effective for several years. Inevitably, cells become castration-resistant and grow strong enough that hormone therapies have a lessening effect on the cancer. However, a number of "secondary" inhibitor and blocker hormone therapies can be used to slow the spread of the disease.

Recent study results show that adding Zytiga® (an inhibitor discussed in the next section) or the chemotherapy drug Taxotere® to initial hormone therapy in men with newly-diagnosed metastatic prostate cancer may improve outcomes.

Inhibitors and Blockers

Even with hormone injections, your cancer may progress to the point where the adrenal glands or prostate cancer cells themselves produce androgens that fuel the cancer's growth. This is when the disease becomes castration-resistant and stronger treatments need to be added to a regimen of injected



There are other treatments in the pipeline for castration-resistant prostate cancer patients.

hormone therapies. New hormonal medications that inhibit the synthesis of androgen, such as Zytiga, and block androgen receptor signaling, such as Xtandi®, received FDA approval with the help of federal research funding supported by ZERO - The End of Prostate Cancer. Each of these drugs is for men with metastatic castration-resistant prostate cancer.

About 10 percent of the body's testosterone is created by the adrenal glands, and few therapies focus on shutting down this production until it becomes absolutely necessary to rid the body of all testosterone. Zytiga is used in combination with steroids to shut down the adrenal glands while avoiding the adverse effects of chemotherapy. As previously mentioned, recent study results suggest a benefit to adding Zytiga to initial hormone therapy for men with newly-diagnosed metastatic disease.

Xtandi blocks androgen receptors to slow the production of testosterone without the use of a steroid.

There are other treatments in the pipeline for castration-resistant prostate cancer patients. See page 12 for more information on current clinical trials.

Side effects of hormone therapies include:

- Breast pain or enlargement
- Cardiovascular events
- Cholesterol level changes
- Erectile dysfunction/lower libido
- Diarrhea and/or constipation
- Increase in belly fat
- Increased risk of osteoporosis

IDENTIFYING TREATMENT OPTIONS

TYPE OF HORMONE THERAPY	WHAT IT DOES	EXAMPLES
Anti-Androgens	Disrupts the interaction of testosterone with cancer cells	<i>Flutamide, Casodex, Nilandron</i>
Luteinizing Hormone Treatment	Shuts down luteinizing hormones that signal the production of testosterone	<i>Lupron, Zoladex, Eligard, Firmagon</i>
Inhibitors	Blocks enzymes and/or proteins from making testosterone	<i>Zytiga, Xtandi, and others in clinical trials</i>

No prostate cancer is the same, and there are many different hormone treatments. Talk to your doctor about which one may be best for you.



IDENTIFYING TREATMENT OPTIONS

RADIATION

Radiation therapy, also called radiotherapy, targets the prostate and specific sites where the cancer has metastasized. It can be used alone or in combination with hormone therapy, chemotherapy, and immunotherapy.

Prostate cancer often spreads to the bones when it progresses. External radiation can be delivered to the affected bone or single area of treatment and can be administered as a series of treatments. Although this type of therapy will not eliminate all cancer cells, it can relieve bone pain and slow the growth of the cancer. It can take up to several weeks after treatment for pain to decrease.

If several areas of the skeletal system are affected and are causing pain, radiation can be administered to the blood stream by injection. Some forms of radiation work like calcium and are absorbed by the bones, most often where there is high bone density. Xofigo® is a new treatment in radioactive medicine for patients with metastatic castration-resistant prostate cancer that works through an intravenous (IV) injection to bring small doses of radiation to the cancer cells in the bone. It uses alpha particles that cause less damage to healthy tissue during treatment while slowing progression and giving some relief to bone pain for a certain length of time.

Targeted radiotherapy is improving in its ability to hit the cancer while leaving healthy tissue alone. See the “Learn” section of the zerocancer.org website for more information about radiotherapy.

IDENTIFYING TREATMENT OPTIONS

Immunotherapy

Unlike vaccines against infections like measles or mumps, immunotherapy is designed not to *prevent* but to *treat* prostate cancer by using the patient's own immune system to fight advanced disease when it becomes castration-resistant.

Currently, there is only one FDA-approved immunotherapy for prostate cancer: Provenge®. It is designed to activate a man's immune cells to best identify prostate cancer cells as abnormal or invader cells in the body. Most prostate cancer cells contain phosphates, which the immunotherapy recognizes and commands the body to attack. The process involves extracting white blood cells from the body and "training" them in a lab to destroy prostate cancer cells. The newly "trained" cells are then injected back into the body a few days later. Since the original cells are from the patient, there is little chance of the body rejecting the therapy. While Provenge can extend the lives of all men, new data suggest that Provenge may be especially effective for African-American men.

Another immunotherapy currently in clinical trials is PROSTVAC. It uses a virus that has been genetically modified to contain PSA, prompting the patient's immune system to respond to the virus and begin to recognize and destroy cancer cells containing PSA. Additionally, some early-phase trials are examining the use of immune checkpoint inhibitors in prostate cancer. Immune checkpoint inhibitors, which are already widely used in many other cancers, work by targeting the molecules on certain immune cells that act as "off switches" to those cells in order to boost immune response.



Chemotherapy

Chemotherapy is typically employed only after all other treatments have failed to manage the progression of the disease. Recent advancements offer new drugs for extending the lives of patients with advanced prostate cancer.

The most widely used and most effective chemotherapy option for advanced prostate cancer patients is Taxotere®. It is administered as an infusion every three weeks over 10 days. Some patients report results within the first three treatments. Another chemotherapy drug, Jevtana®, can be used in combination with prednisone following Taxotere.

Chemotherapy treatments are often administered as part of a regimen to help make the best impact on the cancer while leaving the body time to recover from side effects, which can sometimes be significant.

As previously mentioned, clinical trial results suggest that Taxotere can significantly improve outcomes for men with advanced prostate cancer when added to initial hormone therapy. Visit the "Learn" section of zerocancer.org for more information on these trial results.

IDENTIFYING TREATMENT OPTIONS

Bone Health

Once prostate cancer spreads to the bone, it becomes very painful, but there is hope through treatment. In fact, there are treatments that fight prostate cancer progression to the skeletal system that were not available even a few years ago.

Xgeva® and Zometa® are drugs that stop proteins from signaling bone removal within the skeletal system, and are for patients with bone metastases from solid prostate cancer tumors. The body naturally destroys old bone material while making new bone material. These drugs slow the process of destroying bone material and interrupt skeletal damage to the bones caused by spreading prostate cancer cells.

Xofigo, previously addressed in the radiation section, delivers small doses of radiation to impacted areas in the skeletal system to relieve pain and slow disease progression.



CLINICAL TRIAL OPTIONS

Thousands of men across the U.S. suffer from the difficult effects of prostate cancer and often undergo treatment that does not produce optimal results. If you have prostate cancer, you may feel that your treatment options are limited and you may not know what to do next.

Joining a clinical trial may offer a new avenue of hope. It could prolong your life, improve your health, and enable you to enjoy more quality time with your loved ones.

Here are some currently recruiting clinical trials for men with advanced prostate cancer:



ARAMIS Trial (ODM-201) – For men with high-risk, non-metastatic, castration-resistant prostate cancer.



ATLAS Trial (Apalutamide) – For men with high-risk, localized or locally-advanced prostate cancer.



Enzalutamide + ADT Trial – For men with metastatic, hormone-sensitive prostate cancer.



PROSPER Trial (Enzalutamide) – For men with non-metastatic, castration-resistant prostate cancer who do not experience symptoms of the disease.



S1216 Trial (TAK-700) – For men with newly-diagnosed metastatic, hormone-sensitive prostate cancer.



TRITON3 Trial (Rucaparib) – For men with metastatic, castration-resistant prostate cancer who also have a BRCA1/2 or ATM gene mutation.



VIABLE Trial (DCVAC) – For men with metastatic, castration-resistant prostate cancer who have not yet received chemotherapy.

Visit www.clinicaltrials.gov as a resource for all approved clinical trials.

MANAGING SIDE EFFECTS

TREATMENT	WHAT IT DOES	POSSIBLE SIDE EFFECTS
Hormone Therapy	Minimizes presence of androgens which fuel prostate cancer growth	<i>Erectile dysfunction (ED), hot flashes, bone loss, and cardiovascular events</i>
Radiation	Slows prostate cancer cell growth by targeting cells externally or by injection	<i>ED, incontinence, diarrhea, rectal bleeding and discomfort during urination and bowel movement</i>
Immunotherapy	Changes the body's immune system to kill cancer cells	<i>Fever, chills, fatigue, and joint or body ache</i>
Bone-related Treatments	Inhibits bone loss and fractures and relieves pain from prostate cancer in the bone	<i>Tiredness, diarrhea, nausea, and weakness</i>
Chemotherapy	Targets cancer cells that grow quickly including cancer cells metastasized to the bone	<i>Hair loss, fragile bones, nausea and nervous system disorders like confusion, depression, or headaches</i>

MANAGING SIDE EFFECTS

Minimizing Pain

You can support your own fight against cancer by taking steps to minimize pain. Reducing pain levels makes it easier to think clearly and reduces stress, especially during a treatment regimen. It also reduces the burden on loved ones. Talk to your doctor about pain management, which can include medications, physical therapy, or alternative therapies like acupuncture.

Managing Incontinence

Some patients may already have experience with incontinence as a result of primary treatment like surgery. Incontinence associated with advanced prostate cancer is fairly common with radiation treatment. Kegel exercises help strengthen the muscles in the pelvic floor to combat incontinence.

Additionally, absorbent products, penile clamps, and catheter devices can help you mitigate this side effect. Another solution is a device called a "male sling", which can be used to support the urethra through minimally – invasive surgery. Finally, patients with moderate to high incontinence may wish to consider surgically implanting a urinary sphincter that permits voiding to empty the bladder.

Gaining Intimacy

A common side effect of hormone therapy is the loss of libido. For many, a healthy sex life is important, but depending on your treatment history, solving this issue may be difficult. Medications such as erectile dysfunction (ED) drugs help relax the penis, enabling blood to rush in and an erection to occur.

For difficult cases of ED, a penile implant can be inserted by surgical procedure to put the penis in a permanent semi-rigid state. Another option is an inflatable prosthesis that uses a squeeze-activated pump.

NUTRITION

Studies continue to show a link between prostate cancer and diet. These studies indicate that men who wish to reduce their risk of prostate cancer, as well as men who have already been diagnosed with prostate cancer, may benefit from changing their diet as part of their treatment regimen.



NUTRITION

Specifically, following these dietary principles may be helpful:

1. If it's heart healthy, chances are it's also prostate healthy.
2. Reduce animal fat. Studies show that excess fat, primarily red meat and high-fat dairy, stimulates prostate cancer growth.
3. Avoid trans fatty acids in foods like margarines and fried and baked foods.
4. Increase intake of fresh fish with omega-3 fatty acids, especially cold-water fish like salmon, sardines, and trout. Avoid fried fish.
5. Significantly increase fresh fruits and vegetables. Studies show colorful fruits and vegetables, as well as some nuts and seeds, contain powerful anticancer nutrients. Cruciferous vegetables (cabbage, broccoli, and cauliflower) are protective against cancer. Also, red grapes and products made from red grapes contain flavonoids that inhibit cancer cells.
6. Consume the recommended amount of calcium. Talk to your doctor about the correct amount for you.
7. Add pomegranate juice to your diet. Studies show it may directly reduce PSA.
8. If you take dietary supplements, choose wisely. Discuss all supplements you take with your doctor.
9. Tomatoes, especially tomato products, are rich in lycopene, which is a powerful anticancer substance.
10. Drink green tea several times per week.

QUESTIONS TO ASK YOUR DOCTOR

1. What are the results of my blood work, biopsy, and imaging?
2. What do my current PSA and testosterone levels indicate about my current treatment? How often should we recheck these levels?
3. What criteria do you use to determine treatments?
4. What treatment are you recommending?
5. When do you recommend we start treatment?
6. What kind of results can I expect from this treatment?
7. What are the chances the cancer responds to this treatment?
8. How much time does it take before I can start to see results from the treatment?
9. What are the risks and side effects of this treatment?
10. How do you recommend I manage my side effects?
11. Do you recommend any lifestyle changes? Changes in diet? Exercise?
12. Do you recommend any supplements?
13. How can my loved ones help?
14. Are there any clinical trials that may also be options to consider?
15. What other doctors should I include in the treatment decision-making process? Is it time to talk to an oncologist or get an opinion from a second oncologist?

STAY INFORMED

To find out more about prostate cancer, please visit our website at www.zerocancer.org and click on "Learn." ZERO has online videos, links, and news items about advanced prostate cancer. We also distribute a free electronic newsletter for up-to-the-minute news on treatments, clinical trials, and breakthrough research.

ABOUT ZERO



ZERO — The End of Prostate Cancer is the leading national nonprofit with the mission to end prostate cancer. ZERO advances research, improves the lives of men and families, and inspires action. We're building Generation ZERO, the first generation of men free from prostate cancer, through our national run/walk series, education and patient support programs, and grassroots advocacy. ZERO is a 501(c)(3) philanthropic organization, accredited by the Better Business Bureau, with regional chapters across the country. We dedicate 84 cents of every dollar to research and programs. For more information, visit www.zerocancer.org.

ABOUT ZERO360 COMPREHENSIVE PATIENT SUPPORT



No man should face prostate cancer alone. Now men don't have to. We offer a free service to help patients make treatment decisions, access financial resources to cover treatment and other needs, and find emotional support. Our team of experienced case managers is ready to help you and your family through your personal prostate cancer journey. Contact us toll-free at **1-844-244-1309** or zerocancer.org/zero360



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