

Advanced Prostate Cancer and its Treatment – A Patient Guide

Urologic Oncology Program

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This handout was developed to provide you with general information about the different treatments available for advanced prostate cancer at UCSF. We hope this helps you understand what to expect from, and how to deal with, all aspects of being treated for advanced prostate cancer. Special thank you to all previous contributors to this document. Definitions for words in bold can be found at the end of this document in the glossary.

If you have non-urgent questions related to your health and treatment, please contact your provider through the UCSF online patient portal **MyChart**. If you think you may be experiencing a medical emergency, please call 911 or go to your nearest emergency room. The **MyChart** portal can be accessed at: <http://www.ucsfhealth.org/ucsfmychart>.

Your Feedback

We regularly revise the information presented in this guide so that it is up-to-date and ensure it is as useful as possible for the reader. Because changes and new developments can occur frequently, we suggest you talk to your health care provider for the latest information.

Your feedback about any aspect of this guide would be much appreciated. You can e-mail your comments to urologyresearch@UCSF.edu or send them by regular mail to Your Health Matters Box 1695, UCSF Department of Urology, San Francisco, CA 94143-1695.

If you wish to talk with a Patient Advocate, please call (415) 885-7210.

This guide, along with other urologic oncology documents, can be viewed online with this link: <https://urology.ucsf.edu/prostate-cancer-education-documents>.

If you are reading a hard copy, please refer to the above link for the most up-to-date information.

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Introduction

This handout was developed to provide you with general information about the different treatments available for advanced prostate cancer at UCSF. In general, we define **prostate cancer** as advanced when it requires additional treatment beyond surgery and radiation. Most of the following treatment options are for patients with metastatic advanced prostate cancer. The term metastatic refers to prostate cancer that has spread from the prostate to distant sites, such as bones and lymph nodes. Patients who have no visible evidence of cancer at distant sites, but whose **PSA** is rising after initial treatment, may also be offered some of these treatments; this condition is known as rising-PSA or PSA-only prostate cancer.

Many of the terms below refer to whether or not **hormone therapy** (see more below), which reduces the level of **testosterone**, has been administered, and if it remains effective in controlling the cancer. A person whose disease is responding to hormone therapy is considered to have **hormone-sensitive** prostate cancer, whereas a person whose disease is growing despite hormone therapy is considered to have **castration resistant** prostate cancer or **CRPC**. This term refers to cancer that is progressing despite a testosterone level that is ≤ 50 ng/dL, which is also called the 'castrate range.' The condition is sometimes referred to as hormone resistant prostate cancer.

The UCSF **Genitourinary Medical Oncology** Program has a strong commitment to delivering state-of-the-art health care, improving existing treatments, and developing new therapies for patients with all stages of prostate cancer. UCSF has an extensive clinical trials program that is available to virtually all patients who volunteer and qualify. This handout briefly describes both standard and investigational treatments for prostate cancer. We will provide more information about specific treatment options during your visit. The specific treatment options available to you, including clinical trials, will depend on the treatments already received and your current medical condition.

Overview

Patients with prostate cancer are a diverse population, consisting of those with a prostate-specific antigen (PSA)-only recurrence (with a rising PSA and no demonstrable metastases on imaging) at one end of the spectrum, and those with extensive, high-volume, symptomatic, metastatic disease involving organs and/or bone at the other end. Your choice of treatment is influenced by several factors, including prior therapy, the location and extent of disease involvement, the presence or absence of symptoms, and for patients with nonmetastatic disease (PSA only disease), the prostate-specific antigen (PSA) doubling time.

Hormone therapy is frequently the first treatment offered for patients with metastatic prostate cancer. It is also an option for some patients who choose not to have surgery or radiation for cancer that is confined to the prostate, and for some patients with a rising PSA after surgery and/or radiation. The hormone testosterone promotes growth of prostate cancer. Reducing testosterone levels in the body with hormone therapy can weaken and possibly kill prostate cancer cells. Testosterone is primarily produced by the **testicles**, with a small amount produced by the **adrenal glands**.

There are two treatment options that reduce the production of testosterone from the testicles. One method is to remove the testicles surgically, known as **orchiectomy**. This is rarely done today but remains an option.

The other option is to start **Androgen Deprivation Therapy (ADT)**, which involves medications that very effectively stop the production of testosterone. These include leuprolide acetate (injection: **Lupron**[®]; subcutaneous: **Eligard**[®]), **Zoladex**[®] (goserelin), or **Firmagon**[®] (degarelix). Recently, the FDA also approved **Orgovyx**[®] (relugolix), the first oral testosterone lowering agent, which works in a manner similar to Firmagon[®]. These medications are as effective as orchiectomy in reducing testosterone levels and treating prostate cancer. Side effects of both orchiectomy and the medications can include hot flashes, low sexual desire and erectile dysfunction, fatigue, mood changes, muscle loss, weight gain, anemia, and in some patients on long term therapy, osteoporosis (weakening of the bone). To maintain bone health, we recommend that all patients ask their provider about taking a calcium and/or vitamin D3 supplement. Blood levels should be evaluated, as low vitamin D levels are common, and some individuals require a higher dose of the supplement. Patients should also participate in weight-bearing exercise regularly, as this helps to maintain muscle tone and reduce fatigue. The effects of ADT on metabolism may be responsible for the increased risk of diabetes and heart disease. We strongly recommend aerobic and resistance exercise to maintain cardiovascular health, bone strength and quality of life.

The impact that hormone therapies have on an individual's sex life is equally as important as the other side effects, and we hope to provide an open, supportive environment for you to discuss your conditions and concerns, if you wish. UCSF offers a program for the treatment of erectile dysfunction. For more information, see Managing Erectile Dysfunction - A Patient Guide at <https://urology.ucsf.edu/prostate-cancer-education-documents>.

Patients beginning ADT with Lupron[®], Eligard[®] or Zoladex[®] (as well as the similar drugs **Trelstar**[®], **Vantas**[®] or **Viansa**[®]) will sometimes be given **Casodex**[®] (bicalutamide) for two weeks at the start of therapy to counter a phenomenon known as **testosterone flare** that can briefly cause pain in patients who have metastases in the spine or other at-risk. Casodex is not needed with Firmagon[®] or Orgovyx[®].

ADT is generally the first type of hormone therapy given to an advanced patient. Metastatic patients can continue on ADT treatment for years or even decades. As we will describe below, additional therapy is often combined with ADT early in the treatment for metastatic prostate cancer.

There are a few different strategies for administering ADT. While many patients stay on ADT continuously, some patients are treated with intermittent therapy, which allows them to take a 'holiday' from the therapy. This involves administering ADT until the PSA falls to its lowest point, and then continuing treatment for a total of 9 to 12 months. The drugs are then stopped, followed by careful PSA monitoring,

typically every 1 to 3 months. When the PSA rises to a level predetermined by you and your **oncologist**, the medications are started again for a 9-to-12-month cycle at which point they are again stopped. The PSA is again allowed to rise to a predetermined level, and the cycle continues. The benefit to this approach is that you will be off hormone therapy for a period of time, during which you may experience fewer side effects. We typically do intermittent ADT in patients without metastasis. In patients with metastasis, intermittent ADT therapy is not as effective as continuous therapy. Your provider will discuss with you whether you are an appropriate candidate for intermittent hormone therapy. For more on Hormone Therapy, including helping with side effects see Hormone Therapy for Prostate Cancer - A Patient Guide at <https://urology.ucsf.edu/prostate-cancer-education-documents>.

Please understand that treatment for advanced prostate cancer can disrupt your daily routine, but you should not abandon the principles of diet and exercise that are key to your healthy survival. "Moving Through Cancer: A Guide to Exercise for Cancer Survivors," another Your Health Matters document, is available at: <https://urology.ucsf.edu/prostate-cancer-education-documents>.

Combination Therapy in Metastatic Prostate Cancer

In the past, metastatic prostate cancer was first treated with ADT alone. Advanced treatment would be added to ADT when it no longer controlled the cancer. Although there are still some cases where it is appropriate to start treatment with ADT alone, several studies, beginning in 2017, showed a survival advantage to combining ADT with a more advanced treatment early on in the therapy, before the disease becomes castrate resistant. These combination treatments are described below. Your health care provider will discuss with you the relative benefits and side effects of the treatments that are best medically suited for you. Since some of our therapies are investigational in nature, there may be restrictions placed on situations in which a particular treatment or combination of these treatments can or cannot be used.

In general, combining ADT with one of these drugs started earlier in the treatment regimen will extend the time the disease is kept under control and improve survival. Unfortunately, metastatic disease generally mutates over a number of years and becomes resistant to the combination treatment (the technical term is **hormone refractory**). There are other treatment options that can be applied when this occurs. These are described in later sections. This is a very active area of research.

The three treatments commonly combined with ADT in metastatic therapy are:

1. **Second-Generation Antiandrogens:**

The second-generation antiandrogens were introduced in 2011. Also known as androgen signaling inhibitors, they were originally approved to treat castrate resistant disease, though some are now used for hormone sensitive disease as well.

Abiraterone acetate (Zytiga®) shuts down hormone production in the adrenal gland, and it also prevents highly mutated tumors from manufacturing their own testosterone. It is taken orally once daily in conjunction with **prednisone**. This combination has been shown to prolong survival in patients who have previously received **chemotherapy**, and it is also of great benefit to those just beginning treatment for metastatic or lymph node only prostate cancer. It has been approved by the FDA in both of these settings. Abiraterone is generally well tolerated. Side effects can include increased blood pressure, fluid retention, elevation in liver enzymes, and electrolyte abnormalities.

Xtandi® (enzalutamide) is an antiandrogen pill, and it blocks the stimulating effects of testosterone on prostate cancer cells. In patients who have previously received chemotherapy, Xtandi® has been shown to improve survival, PSA response, and tumor response when compared to placebo. Xtandi® is FDA approved for patients with metastatic prostate cancer, whether they are hormone sensitive or not. It's also approved for patients who experience a rising PSA while they are on ADT, even if no metastasis has been detected. The drug is taken daily by mouth and is well tolerated. There

were rare reports of seizures in patients treated with Xtandi®. You should discuss any prior history of seizures with your healthcare provider.

Erleada® (apalutamide) is another antiandrogen pill that blocks the effects of testosterone. It significantly improves survival in patients who are metastatic yet still hormone sensitive, or who are resistant to hormone therapy with the only evidence of disease being an elevation in PSA. Erleada® is FDA approved for these patients. Side effects include high blood pressure, elevation in glucose levels, elevation in cholesterol levels and increased falls, particularly in the elderly.

Nubeqa® (darolutamide) is an antiandrogen that has fewer neurological side effects compared to other antiandrogens as it does not cross the blood brain barrier. It is currently approved by the FDA for use in patients with hormone resistant prostate cancer where the only evidence of disease is a rising PSA. The drug is taken by mouth twice daily.

Less commonly, other medications (e.g., Casodex®) are used.

2. Chemotherapy:

Chemotherapy refers to drugs that directly kill prostate cancer cells. Usually, these medicines are given intravenously in our infusion clinic. Many hospitals typically offer newly diagnosed metastatic patients a choice between ADT plus chemotherapy or ADT plus a second-generation antiandrogen.

Docetaxel (Taxotere®) is a chemotherapy given intravenously every 3 weeks in conjunction with prednisone (which is taken orally twice daily). The standard duration of treatment is 6 cycles, for a total of 18 weeks. The combination of docetaxel and prednisone has been shown to prolong survival in patients with metastatic CRPC as well as in those who have newly diagnosed metastatic prostate cancer and are initiating ADT. In patients with CRPC approximately 50-60% of patients treated with docetaxel will have a significant decrease in PSA, and 20-40% will have shrinkage of measurable tumors. Side effects may include neuropathy (nerve damage that usually occurs after many doses, typically described by patients as numbness or tingling in the fingers and toes), fatigue, fluid retention, and nausea.

Cabazitaxel (Jevtana®) is a chemotherapy option for patients with or without prior treatment with docetaxel. Like docetaxel, cabazitaxel is given every 3 weeks in conjunction with prednisone taken twice daily. The combination of cabazitaxel and prednisone received FDA-approval for the treatment of **metastatic** hormone-refractory **prostate cancer** in patients who have already received docetaxel, having shown improved survival in these patients. Major side effects may include diarrhea, low blood counts, and impairment of the immune system that may put you at risk for serious infections. Due to the risk of infection during the time when you are neutropenic (when your white blood cell count is low, usually 7-10 days after receiving cabazitaxel), cabazitaxel is often given with a medication called Neulasta® that can boost the immune system. There are other chemotherapeutic options than can be used after (or in combination with) docetaxel and cabazitaxel. While these drugs have not been shown to improve survival, they can be effective for some patients, to help control symptoms and has been, and has been shown to provide tumor reduction or stability in some patients. Your health care provider will discuss these options if they are medically suited for you.

In certain cases, your oncologist may add another chemotherapy drug called **Carboplatin** (Paraplatin®) to either of the chemotherapy medications above.

3. Treatment to the primary tumor and oligometastases

Until recently, patients who were metastatic when they were diagnosed were not offered radiation therapy or surgical removal of the prostate (**prostatectomy**). A recent randomized controlled trial has shown that for patients with a low metastatic burden, radiation treatment to the prostate can result in a significant survival benefit. For patients with a higher metastatic burden, no such benefit has been observed.

In addition, with advances in imaging and precision radiation techniques, it is possible to characterize the extent of metastases and treat them with targeted radiation or surgery if the number of detected metastases is fewer than 5 (**oligometastatic** patients). Studies have also shown a survival benefit when metastasis is confined to the **pelvic lymph nodes** (regionally advanced). Studies which treat more distant metastases are ongoing, but they have not yet yielded conclusive results.

Advanced Therapies for Metastatic Prostate Cancer

There are three additional types of therapy that can be used to treat prostate cancer if the cancer progresses despite the combination therapies described above:

1. Immunotherapy:

These agents have the potential of stimulating your body's own immune system to fight the cancer. These treatments are usually well tolerated but may not be effective for everyone.

Provenge[®] (Sipuleucel-T) is a cell-based therapy that stimulates your immune system to fight against prostate cancer. Each Provenge dose must be custom-made for each individual patient: first, patients have their blood run through a machine in an outpatient infusion center for 2-3 hours to extract certain immune cells. These immune cells are then mixed with a protein that is commonly found on prostate cancer cells to sensitize the immune cells to the cancer. The mixture is then returned to the patient in a 1-hour infusion, given two days after the immune cells were extracted. The whole process is repeated two more times over the course of a month. This process alerts your immune system that prostate cancer cells should be attacked as if they were foreign invaders. In clinical trials in patients with hormone refractory prostate cancer, those who received Provenge[®] lived an average of 4 months longer than those who did not. Some patients were alive 3 years later. Interestingly, patients who lived longer with Provenge did not have reductions in PSA or shrinkage of their tumors. Side effects of Provenge[®] are mild, including flulike symptoms that resolve within a few days, and rarely, allergic reactions at the time of infusion.

Keytruda[®] (pembrolizumab)

Keytruda[®] has shown benefit in several advanced cancers that have abnormal **DNA** repair mechanisms. This results when genes that regulate DNA (also called Mismatch Repair Genes) do not work correctly. The Mismatch Repair genes work like the body's "spell checkers" and correct errors in DNA. When these genes stop functioning normally, errors in DNA are not repaired, resulting in the cancer cells becoming "unstable" and therefore more likely to respond to Keytruda[®]. The FDA approved Keytruda[®] for the treatment of advanced cancers (including prostate) that have deficient mismatch repair, and which continue to progress when all other treatment options have been exhausted. Keytruda is especially effective in patients whose tumor biopsy shows an indication labeled as 'MSI high.'

Keytruda is also being applied with other therapies in clinical trials because it can help the body's own immune cells to penetrate the cancer's defenses.

2. Radio-Isotope Therapy:

Radium-223 (known as Xofigo[®]) is a radioactive drug that can be taken up in the bones in place of calcium (radium is chemically similar to calcium). Once it's incorporated into the bone, Radium-223 emits radiation that can kill nearby metastatic cells growing within the bones. A study with Radium-223 demonstrated that administering 6 treatments with this isotope can decrease bone related complications of the cancer as well as improve survival. It is typically used in patients who have already received chemotherapy or who are not deemed healthy enough for chemotherapy. Radium-223 is injected intravenously and it targets areas of bone that are being damaged by the cancer. Side effects of Xofigo are mild for most patients. However, it is important to note that the patient's bone marrow health needs to be monitored with regular blood tests. Some patients experience mild diarrhea.

An emerging area of research in radio-isotope therapy targets a protein called PSMA (prostate specific membrane antigen). This protein grows on the surface of prostate cancer cells. Over the past decade, novel molecules have been developed which can attach radioactive isotopes to prostate cancer cells by targeting their PSMA proteins. When the isotope **Gallium-68** is used this way it permits a PSMA-PET scan to detect the cancer cells with much more accuracy and sensitivity than previous technologies offered. When the radioactive isotope **Lutetium-177** is attached to the cells' PSMA, it damages and eventually kills the cancer cell. Some prostate cancer cells (approximately 5-10%) do not express PSMA on their surface and will not show on a PSMA-PET scan. These cells can survive treatment with PSMA directed Lutetium-177.

PSMA imaging with Gallium-68 was approved by the FDA in December 2020 for use at UCSF and UCLA (and eventually other institutions). Although the corresponding treatment with Lutetium-177 has not yet been approved by the FDA, the clinical trial of Lutetium-177 has reported positive findings and so it will hopefully be approved by the FDA in the near future. UCSF has several clinical trials utilizing PSMA as a diagnostic and therapeutic tool, including a study which combines Lutetium-177 with Keytruda®.

3. DNA repair targeting:

When a cell's DNA is damaged, a mechanism within the cell tries to repair the DNA. About 25% of patients with hormone resistant disease have gene mutations which disable this repair mechanism (some are born with the mutation, and some acquire it later in their cancer cells). The most commonly mutated genes include BRCA1, BRCA2, ATM and CHEK2. Fortunately, patients with these mutations can be treated with a chemotherapy called carboplatin or with a class of drugs called PARP inhibitors. Among these, patients with BRCA2 mutations appear to benefit the most from PARP inhibitors.

Olaparib (Lynparza®) and rucaparib (Rubraca®) were recently approved for treatment in patients with castrate resistant prostate cancer associated with mutations in one of the above genes. Your health care provider will discuss these options if they are medically suited for you.

Investigational Therapies

There are many opportunities to participate in clinical trials at UCSF, some of which include investigational agents. Others include the FDA-approved therapies described above, using them in novel ways or in combination with investigational agents. For example, at UCSF, Zytiga® and Erleada® in combination with ADT are being compared to Erleada® with ADT versus ADT alone in the patients with hormone sensitive cancer who have rising PSA after surgical removal of the prostate.

Investigational trials at UCSF include:

- Niraparib: this drug is not currently FDA approved. The combination of Niraparib and abiraterone/prednisone will be compared to abiraterone/prednisone only in patients with hormone sensitive prostate cancer with defective DNA repair genes.
- Keytruda® plus Docetaxel: Keytruda® works by unleashing your body's immune cells against cancer. Both of these drugs are individually approved by the FDA, but the combination is currently being investigated in the KEYNOTE 921 study in patients with hormone resistant prostate cancer.
- BXCL701: this is a novel drug that stimulates the immune system and is currently being investigated in combination with Keytruda® in castrate resistant prostate cancer and small cell neuroendocrine prostate cancer.
- PSMA: We have several trials utilizing PSMA as a diagnostic and therapeutic tool in combination with other drugs like Lutetium and Keytruda®.

- HPN424: This novel agent works by engaging the **T lymphocytes** with PSMA on prostate cancer cells.
- JNJ-63898081: This is another antibody that binds to T lymphocytes and PSMA on prostate cancer cells and is currently being evaluated in patients with castrate resistant prostate cancer.
- Erleada®: this is being evaluated in combination with radiation in patients with limited castrate resistant prostate cancer.
- FOR46: This is an **antibody drug conjugate** that specifically targets the protein CD 46 which is commonly expressed in castrate resistant prostate cancer. It is given intravenously every 3 weeks.
- Bipolar Androgen Therapy (BAT) and Keytruda®: BAT is a novel approach to treating metastatic prostate cancer by flooding the cancer cells with testosterone while the patient is on ADT, and then waiting four weeks to allow the testosterone level to return to castrate level. The combination of BAT and Keytruda® is hoped to provide more benefit than either therapy alone.

Accessing and Analyzing Metastasis

UCSF has a large program designed to obtain biopsies from sites of metastatic disease such as the bone and liver, from patients with metastatic prostate cancer. A large part of our research is aimed at being able to more accurately describe the types and subtypes of prostate cancer that evolve during months and years of treatment. Obtaining these biopsy tissues may eventually enable us to tailor therapies for patients. Your health care provider may discuss your participation in one of these biopsy programs. UCSF also has a number of experimental programs designed to analyze tumor cells that are circulating in the blood. Many of these techniques (circulating tumor cells, cell free DNA and others) are done as part of other experimental protocols. In general, most clinical trials require that your prostate cancer is progressing to be eligible. If you are responding to a particular treatment, participation in a clinical trial might not be possible at the present time but may be appropriate in the future. UCSF also has an extensive clinical trials program. Your health care provider will discuss any trials for which you may be eligible to participate.

Additionally, UCSF has a large Phase I/Developmental Therapeutics program led by an experienced multidisciplinary team. In general, phase I trials evaluate the safety of new pharmaceutical compounds in a small number of patients. If you participate in a phase I trial, you will see an oncologist who specializes in phase I trials in conjunction with your current oncologist.

Other Therapies

Denosumab (Xgeva®) is a medication that is used to strengthen the bones. It has been shown to reduce the rate of bone-related events (e.g., fractures, bone pain, new bone lesions) in patients with hormone refractory prostate cancer who have bone metastases. Xgeva® is given by injection monthly. Xgeva® can lower calcium and phosphorus levels in your blood, so these blood levels must be checked before each dose.

Xgeva® should be taken in combination with a calcium and vitamin D3 supplement. Xgeva® can occasionally cause a condition called osteonecrosis (bone damage) of the jaw. If you are currently undergoing or planning dental work (routine cleaning is not a risk), please discuss this with your provider and dentist.

A group of medicines called *bisphosphonates* can also be used to prevent thinning of the bones.

This document is a general overview of possible treatment options. We will be providing you with considerably more information as we discuss the treatment options that are best medically suited for you. Our primary commitment is your well-being. Please let us know if there is more information that you need.

Appendix: Summary Of FDA Approved Treatments

The following table shows which treatments are appropriate for treating advanced prostate cancer, depending on whether the cancer is sensitive to androgen deprivation therapy and whether distant metastases are present. Please note that these are general guidelines and final decisions are made by the health care provider in consultation with the patient.

Disease State	ADT Sensitive	ADT Resistant	Usage Notes
No Metastases	Lupron®	Lupron®	Androgen Deprivation Therapy (ADT) ¹
	Eligard®	Eligard®	ADT
	Zoladex®	Zoladex®	ADT
	Firmagon®	Firmagon®	ADT
	Orgovyx®	Orgovyx®	ADT
		Xtandi®	Antiandrogen
		Erleada®	Antiandrogen
		Nubeqa®	Antiandrogen
	Prolia®	Prolia®	Osteoporosis ²
Metastases	Lupron®	Lupron®	ADT ¹
	Eligard®	Eligard®	ADT
	Zoladex®	Zoladex®	ADT
	Casodex®		Often used briefly when starting Lupron®, Eligard®, or Zoladex® ¹
	Firmagon®	Firmagon®	ADT
	Orgovyx®	Orgovyx®	ADT
	Zytiga®	Zytiga®	Antiandrogen (hormone suppressant, generic: abiraterone)
	Xtandi®	Xtandi®	Antiandrogen
	Erleada®		Antiandrogen
		Taxotere®	First line chemotherapy (generic: docetaxel)
		Jevtana®	Second line chemotherapy (gen: cabazitaxel)
		Paraplatin®	Can be added to chemotherapy
		Provenge®	Immunotherapy
		Keytruda®	Microsatellite instability (MSI) high
		Lynparza®	DNA damage repair (generic: olaparib)
		Rubraca®	DNA damage repair
	Xgeva®	Xgeva®	Osteoporosis and bone metastases in ADT resistant disease ²
	Xofigo®	Radium infusion for symptomatic bone metastases (Ra-223)	

Note: Shaded cells are oral medications; unshaded cells are injections.

1. Trelstar® Vantas® and Viansa® are similar ADT drugs, omitted for brevity
2. Bisphosphonates (e.g., Zometa® and Fosamax®) can also be used for bone health

Glossary

Abiraterone acetate (Zytiga®) - a drug that blocks the final step in the body's production of testosterone, particularly in the adrenal glands and internally within a prostate cancer cell. Taken with prednisone.

Actinium-225 – a radioisotope which is similar to Lutetium-177; Ac-225 emits more powerful radiation and has more side effects.

Adrenal glands - small glands located on top of each kidney which produce a small amount of testosterone (and other hormones).

Androgen - a hormone which stimulates the development of male characteristics, generally testosterone or the more potent dihydrotestosterone.

Androgen deprivation therapy (ADT) - the disruption of testosterone production in the testicles through the administration of drugs like Lupron® or Firmagon®.

Antiandrogen - a drug which prevents testosterone from stimulating prostate cancer cells, generally added to ADT either at the start of therapy or when the cancer progresses.

Antibody drug conjugate – a treatment that combines (conjugates) an antibody (which can attach to a cancer cell) with a drug that can kill the cancer cell.

Biopsy - the collection of tumor tissue from a patient, generally through needle aspiration.

BRCA1, BRCA2, ATM and CHEK2 - four genes whose mutations can be targeted for prostate cancer treatment.

Cabazitaxel (Jevtana®) - a chemotherapy drug which is generally used after docetaxel.

Carboplatin (Paraplatin®) - a drug which can be added to chemotherapy in aggressive cases.

Casodex® (bicalutamide) - a first generation antiandrogen which is sometimes used for short term therapies.

Castration resistant prostate cancer (CRPC) - prostate cancer which can grow in a low testosterone environment (i.e., during androgen deprivation therapy).

Chemotherapy - a form of cancer treatment in which chemicals which are toxic to cancer cells are infused into a patient's bloodstream. Can be used as the first therapy in metastatic prostate cancer or after other therapies stop working.

DNA - Deoxyribonucleic acid in a cell's nucleus which contains a blueprint for constructing all of an organism's proteins. Cancers often develop when a cell's DNA mutates (is altered) in a manner that removes normal regulators of cell growth.

Docetaxel (Taxotere®) - a chemotherapy drug which is generally the first one used to try and destroy prostate cancer through cytotoxicity (toxicity to cells).

Eligard® (leuprolide acetate) - an androgen deprivation therapy (ADT) drug which is injected under the skin to form a depot which continually delivers the medication for a 1, 3, 4, or 6-month period.

Erleada® (apalutamide) - a modern, second generation antiandrogen approved by the FDA for prostate cancer.

FDA - the US Food and Drug Administration which carefully reviews clinical trials and certifies the level of safety and efficacy for medical treatments.

Firmagon® (degarelix) - one of the main ADT drugs, it has the fewest cardiovascular side effects and fastest testosterone reduction and subsequent recovery after discontinuation. It must be injected monthly into the belly fat which can be problematic.

Genitourinary Medical Oncology - the group in an oncology department which treats male reproductive cancers and cancers in the urinary systems (including kidneys) for males and females.

Hormone refractory - prostate cancer which can grow despite treatment with ADT and advanced antiandrogens (e.g., Zytiga®, Xtandi®, Erleada®, Nubeqa®).

Hormone-sensitive prostate cancer - prostate cancer which can be controlled by reducing testosterone levels in the body.

Hormone therapy - a broad category of treatments that includes both ADT drugs (which suppress testosterone production in the testicles) and antiandrogens (which prevent testosterone from stimulating prostate cancer cells)

Immunotherapy - cancer treatments which try to harness the body's own defenses to fight cancer, generally by stimulating t-cells to attack the tumors.

Intermittent ADT – ADT which is taken by a patient for up to a year or so, followed by a break for several months after the PSA settles down to its lowest level.

Keytruda® (Pembrolizumab) – a checkpoint inhibitor, Keytruda® can be effective against cancers that have a certain genetic defect (called 'MSI high'), and can also help the body's immune system overcome some of the defenses mounted by the cancer cells.

Lutetium-177 – a radioactive isotope which can be bound to a molecule which will attach it to a cancer cell where it can kill the cell. In prostate cancer Lu-177 commonly targets the PSMA protein on the cell surface.

Lupron® - a testosterone reducing hormone which is injected intramuscularly every 1,3, 4 or 6 months.

Metastasis – a colony of cancer cells which grows in a site beyond their origination organ. A prostate cancer metastasis can be visceral, which means they are growing in soft tissue, or osseous, which means they are growing in bone tissue.

Neuropathy – pain or a loss of sensation in nerves. Neuropathy can be a side effect of chemotherapy.

Nubeqa® (darolutamide) - the most recent second-generation antiandrogen to be approved by the FDA. It has fewer neurological side effects since it does not cross the blood-brain barrier.

Olaparib (Lynparza®) and **rucaparib** (Rubraca®) – drugs in a class called PARP Inhibitors, these drugs help treat patients whose cancer has a defect in the BRCA-2 gene, among others.

Oligometastases – small numbers of metastases (generally fewer than 5 in total), which may be treatable by radiation.

Oncologist – a doctor who specializes in cancer treatments. In prostate cancer, a medical oncologist will generally supervise your anti-cancer medications. A radiation oncologist will supervise any radiation treatments you receive. A urological oncologist will supervise any surgery you may need.

Orgovyx® (relugolix) – the only ADT treatment which can be taken in pill form instead of injection. Orgovyx® works in a manner similar to Firmagon® to quickly reduce testosterone to very low levels.

Orchiectomy – the surgical removal of the testicles in order to reduce testosterone production to a very low level.

Pelvic lymph nodes – lymph nodes within the pelvic area. These nodes are also called regional lymph nodes. Cancer which has spread, but is confined to the pelvic nodes, is called regionally advanced prostate cancer.

Prednisone – a steroid which can reduce inflammatory responses. Prednisone is often given with chemotherapy or Zytiga®

Primary tumor – in prostate cancer, any tumor within the prostate gland.

Prostatectomy - surgical removal of the prostate. Prostatectomy was originally reserved for non-metastatic patients, but some recent studies are investigating the possible benefits for oligometastatic patients.

Provenge® (Sipuleucel-T) – One of two FDA approved immunotherapies for prostate cancer. Provenge® treatment consists of the extraction of certain immune system blood cells from the patient, followed by treatment to the cells to sensitize them to cancer cells. These treated cells are infused back into the patient.

PSA – prostate specific antigen. All prostate cells produce PSA. Prostate cancer cells generally produce more PSA than normal cells, but there is much variation. After prostatectomy the PSA should be undetectable. Any measurable PSA following the surgery is a sign of likely recurrence. A rise in the level after radiation treatment likely indicates recurrence as well.

PSMA – prostate specific membrane antigen. These proteins preferentially grow on the surface of prostate cancer cells (as well as a few other sites like the salivary glands). PSMA proteins can be used as targets for radioactive isotopes which can identify cancer cells on a PET scan (imaging). These proteins are also used as targets to deliver treatment to tumor cells (therapy).

Radio-Isotope Therapy – therapy that uses radioactive isotopes to treat cancer. In prostate cancer, the isotopes Actinium-225, Lutetium-177, and Radium-223 are the most frequently used (only Radium-223 is FDA approved as this is written).

Radiologist – a medical doctor who specializes in medical imaging. This person is different from a radiation oncologist, who plans and directs radiation therapy.

Radium-223 (Xofigo®) – Isotope for treating prostate cancer which has metastasized to the bone. Xofigo® can be infused to relieve pain and possibly slow down the progression of the disease.

Regionally advanced – prostate cancer which has spread to the pelvic lymph nodes, but not to other organs, bones, or more distant nodes. In clinical research and treatment, a distinction is made between patients with regionally advanced prostate cancer and patients with distant metastases.

Survival benefit – in a clinical trial, the survival benefit is measured as the increased months or years of survival for the patients who receive the treatment being studied.

T lymphocytes (also called T cells) - type of white blood cell which can detect foreign cells (like cancers) and then bind to the cell and kill it. Unfortunately, T cells have had only limited success in the fight against prostate cancer. Research is continuing in the area called immunotherapy.

Testicles – the glands beneath the penis which manufacture almost all of the male body's testosterone.

Testosterone – a hormone which is responsible for stimulating the development of male sexual features such as, body hair and muscle and bone mass. It also plays an important role in stimulating the development of prostate cancer. Testosterone is also present in a more potent form, known as dihydrotestosterone.

Testosterone flare – a brief rise in testosterone following the initiation of ADT with drugs like Lupron® or Eligard® (but not with Firmagon® or Orgovyx®), which can increase pain and possibly cause injury to patients with advanced metastases.

Trelstar® (triptorelin) - an ADT therapy which is similar to Lupron and is injected into a muscle every 4, 12 or 24 weeks.

Vantas® (histrelin) – an ADT therapy which is surgically administered as a tiny implant under the skin of the upper arm. It lasts for a year and must be surgically removed or replaced.

Viadur® (leuprolide) -an ADT therapy which is similar to Lupron® but administered as an implanted dispensing device in the upper arm, which is replaced annually.

Xtandi® (enzalutamide) - a second generation antiandrogen approved by the FDA which on rare occasions can cross the blood-brain barrier and cause seizures.

Zoladex® (goserelin) - an androgen deprivation therapy (ADT) drug which is administered as a small pellet in the belly area which slowly dissolves to release medication for a 1 or 3-month period.