

Advanced Prostate Cancer PDF

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c2024

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What is cancer?

A cancer is also called a malignant tumor. Cancer cells begin in one body part and grow there before spreading to other parts of the body.

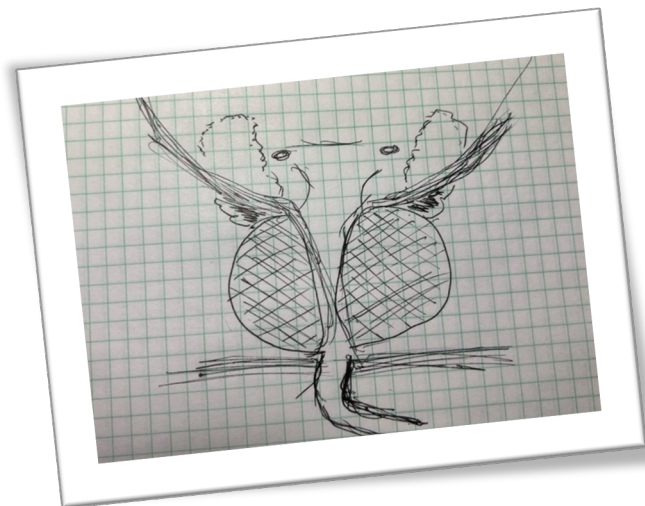
All cancer cells have four basic characteristics.

1. Cancer cells grow without stopping or differentiating themselves into a useful purpose.
2. Cancer cells can invade and spread into other organs and continue to grow.
3. Cancer cells evade detection or destruction by the body's natural immune system that would otherwise destroy the bad cells.
4. Cancer cells produce growth factors that encourage new blood supply and destruction of other tissues that allows the tumors to grow.

What is prostate cancer?

Prostate cancer is a cancer that begins in the prostate. Prostate cancer is typically an adenocarcinoma that starts in the prostate and then spreads to other parts of the body.

Prostate cancer grows with a wide variety of cell types, from non-aggressive slow growing cancers that tend to stay confined to the prostate to faster growing aggressive tumors. The GRADE of a prostate cancer (Gleason Score or Grade Group) is a prediction of the future behavior of the cancer.



The prostate sits below the bladder and above the muscle floor of the pelvis. Urine flows from the bladder through the prostate and into the urethra. Prostate cancer begins in the prostate then spreads to other

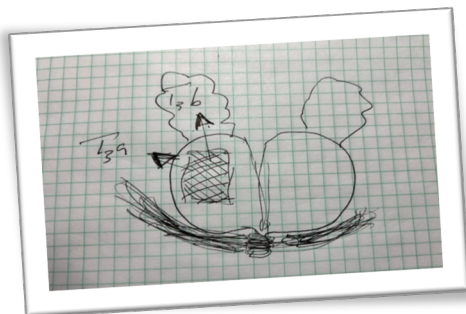
What is advanced prostate cancer?

Advanced prostate cancer is any cancer that has advanced beyond the prostate. When a prostate cancer has spread to another body part it has metastasized. Metastatic is a word used to describe cancers that have spread beyond the organ where the cancer started.

The advanced disease can be local advancement, or it can be widespread metastatic disease. In the case of prostate cancer local advancement is to surrounding body parts, the bladder, rectum, neurovascular connective tissue, and pelvic floor muscles.

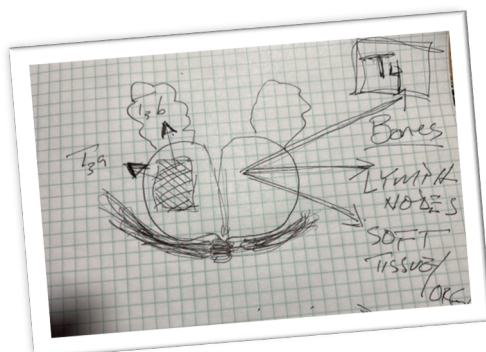
Locally advanced disease can often be treated with primary treatments such as radiation or possibly surgery. Locally advanced disease will have a higher chance of cancer recurrence after primary treatment than cancers that are confined to the prostate.

Local advancement is stage 3, extending beyond the capsule and or to the seminal vesicles.



Here is a picture of the prostate with a tumor represented by the hash-marked rectangle. A tumor that spreads through the edge of the prostate is a stage T3a. A tumor that spreads into the seminal vesicle is stage T3b.

Widely metastatic Cancer is stage 4. Patient with advanced stage 4 disease will need systemic treatment.



Metastatic prostate cancer is Stage 4. Prostate cancer spread can be differentiated into 3 potential types:

1. Bone
2. Lymph Nodes
3. Soft tissue/Organs

Treatment options will be dependent on the type of spread. Spread to lymph nodes is common, often treated with androgen deprivation. Spread to bones may require radiation to the affected area. Metastasis to soft tissue requires more aggressive therapies.

What tests are used to detect metastatic or advanced prostate cancer?

PSA blood test: The PSA blood test is the most common way that a cancer will be detected. Risking PSA test after primary treatment is the most common way a cancer is detected. Also, the doubling time (how fast a PSA doubles in value) often determines how aggressive treatment is needed.

PSMA PET scan: A PET scan uses a radiotracer to detect cancer. The PSMA scan is the most sensitive test to best detect recurrence or metastatic cancer.

MRI: An MRI gives a very detailed picture of soft tissue using a powerful magnetic field to create the image.

Bone Scan: A radiotracer can be given that targets abnormal bone tissue. This type of image is less sensitive than a PET scan but is useful in specific cases

CT scans: CT stands for computed tomography. A computer collects data from multiple x-ray images to create a detailed picture. CT scans a very common tests and useful in many circumstances to detect cancer recurrence.

Biopsy: A biopsy of any tissue found is often helpful to determine the next course of action.

What are the options typically used for treatment of metastatic prostate cancer?

Radiation: Radiation treatments can be used selectively to target specific areas of recurrence, especially to areas of bone that are symptomatic or may cause symptoms in the future.

- External beam radiation to specific metastases
- Radium 223 for systemic, symptomatic metastases
- Lutetium directed radiation targets the expression of PSMA on the cell surface through directed antibody treatment.

Androgen Deprivation (Hormones): Suppression of testosterone is the most common form of treatment of prostate cancer.

- Injections of long acting (3-6 months) testosterone lowering medication, leuprolide is injected intramuscular (Lupron) or under the skin (Eligard).
- Oral medication (Orgovyx) is a newer agent suppressing testosterone.

- Androgen synthesis inhibitor (Abiraterone) can be combined with androgen suppression.
- Androgen receptor inhibitors (Enzalutamide, Apalutamide, Darolutamide) are combine with androgen suppression.

Chemotherapy: Chemotherapeutic agents are used for advanced disease, especially in cases of soft tissue organ involvement which indicates very aggressive disease.

- Chemotherapy options such as docetaxel and cabazitaxel are combined with androgen deprivation and second line agents in a triple therapy regimen.
- Special medication such as Olaparib and Rucaparib are used with specific genetic alterations within the tumor.

Immunotherapy: Immunotherapeutic agents are being used in experimental protocols.

- Sipuleucel-T is given for patients with metastatic hormone resistant cancer.
- Lutetium uses antibodies against expressed PSMA on the surface of cancer cells to direct radiation therapy to the cancer cells.

What is sequencing of prostate cancer treatments?

Recurrence of prostate cancer can be local or advanced. A local recurrence is cancer growing back where the prostate used to be (in the case of prostatectomy) or in the prostate itself if the cancer was treated with radiation initially. Advanced or metastatic disease is cancer that has spread to obvious growth in other places in the body

A PSA recurrence after definitive treatment such as removal or radiation may not require treat. This is dependent on the growth of the recurrence. Slow growing cancers do not necessarily need treatment.

A doubling time of greater than 12 months (how long it takes the PSA to double) is a surrogate for tumor volume and tumor growth.

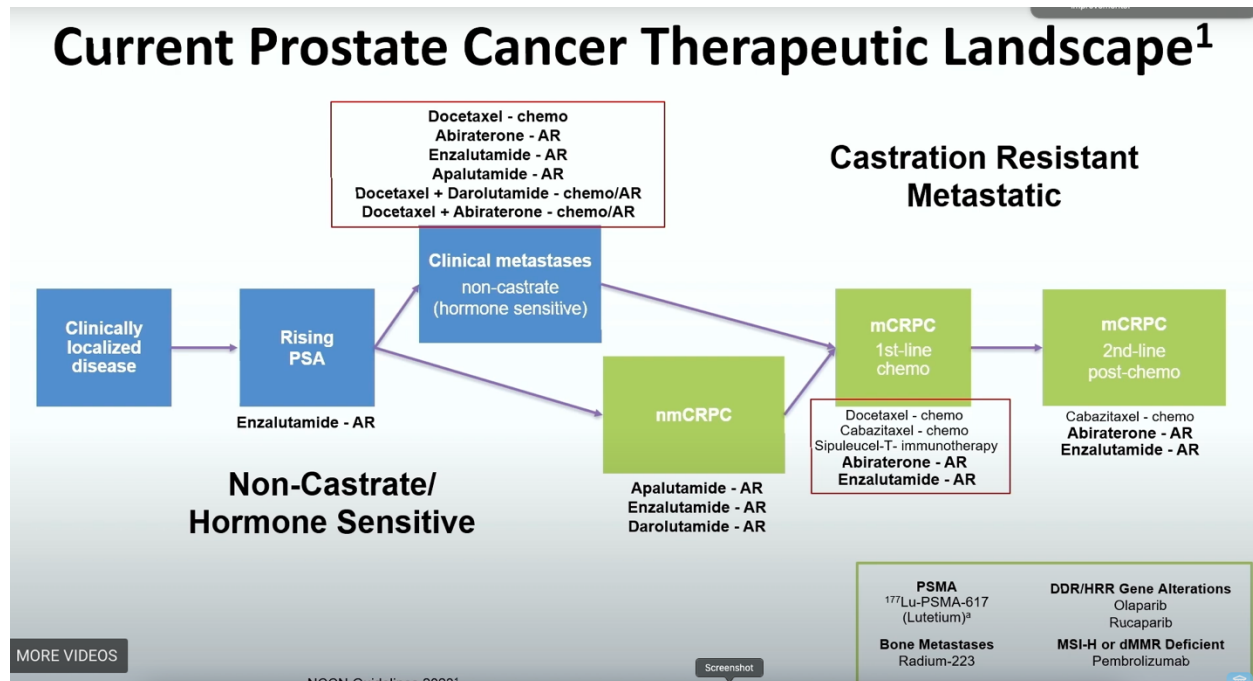
Slow PSA recurrence may be able to be monitored over time, with serial PSA testing, exams and imaging.

How high can a PSA get before we need to give a man treatment? This is a question that is difficult to answer. Elderly men or men with significant health concerns can allow the PSA to get higher because given their expect longevity. Younger and healthier men need closer surveillance and more frequent discussion about what intervention is best.

In time, however, a PSA recurrence must be treated. Recurrence will eventually declare itself in the form of a metastatic lesion with lymph node involvement (lymphadenopathy), bone metastasis or spread to an organ such as liver or lung.

What are the options?

Your individual circumstance will determine your next step. Here is a simple algorithm based on current discussion/education from the AUA. Below is a screenshot of a slide from a lecture.



If a man has a PSA recurrence felt to be localized to a recurrence in the pelvis after prostatectomy, most often he will be advised to undergo radiation treatments to the pelvis to try to control the local recurrence. That may or may not need additional therapy.

If a man has a local recurrence in the prostate after prior treatment such as radiation, cryotherapy or HIFU this is a special circumstance. Previous treatment with radiation most often precludes the ability for prostatectomy; the surgery is made difficult by the scarring after radiation. Prior HIFU or cryotherapy treatments may still allow for prostatectomy depending on the clinical scenario.

If a PSA has a faster doubling time (less than 6 months) most men will be advised to begin treatment with androgen deprivation (pills or injection/shot) along with an additional testosterone synthesis inhibitor (abiraterone) or androgen receptor blocker (enzalutamide, darolutamide, apalutamide)

If a hormone sensitive prostate cancer presents with metastatic lesions typically a chemotherapy called docetaxel is used in combination with the prior treatments.

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When the prostate cancer becomes castrate resistant (growing despite androgen deprivation) additional treatments are added such as Sipuleucel-T, cabizatxel, docetaxel.

Special treatment options as of 2024

The options listed below are used less commonly in 2024 but I suspect will be used more and more as we learn about the potential of these treatments, or of treatments that derive from these options.

If PSMA positive, then Lutetium treatments can be considered. Currently this is by experimental protocol only.

If DDR/HRR gene alterations, then consider Olaparib and Rucaparib. Genetic variants are determined by genetic testing of the prostate cancer.

If bone metastases symptomatic, then consider Radium-223. These treatments are delivered by the radiation oncologists. This treatment is used for very symptomatic bony metastases.

If MSI-H or dMMR deficient. then consider Pembrolizumab. Genetic variants are determined by genetic testing of the prostate cancer.