Improving Prostate Cancer Patient Care in the Clinical Setting

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Presenters' disclosures of conflicts of interest are found at the end of this article.

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Abstract

At JADPRO Live 2023 in Orlando, presenters provided an overview of best practices in the diagnosis, classification, and management of patients with localized and metastatic prostate cancer. They covered selecting appropriate therapies based on patient clinical presentation and treatment goals, as well as managing side effects and interventions for modifiable health risks in patients with prostate cancer.

Recent research has advanced our understanding of the treatment of prostate cancer. At JADPRO Live 2023, Jessica Deinert, MSN, APRN, FNP-C, AOCNP®, and Leah K. Shaw, MSN, APRN, AGPCNP-BC, both from the department of GU medical oncology at The University of Texas MD Anderson Cancer Center, provided a detailed overview of prostate cancer diagnosis and management with a focus on patient-centered decision-making.

Prostate cancer is the most commonly diagnosed cancer among men, and it is the second-leading cause of cancer-related death among men. In 2023, there were an estimated 288,300 new diagnoses of prostate cancer with 34,700 of those cases resulting in death (American Cancer Society, 2023). Of patients who are diagnosed with prostate cancer, about 69% of them are diagnosed with localized disease. Another 13% have regional disease and about 8% have metastatic disease.

STAGING

The most widely used staging system is TNM staging. Clinicians will assess for nodal involvement as well as metastatic sites. At the time of biopsy, cells are assessed for a Gleason score, and at times a grade group that corresponds with the Gleason score is also reported.

Anatomic imaging used for staging includes an MRI pelvis, CT chest, abdomen, and pelvis with a bone scan, or in some cases a prostate-specific membrane antigen (PSMA) PET/CT, a modality specific to prostate cancer at the time of diagnosis.

"It is best to use a prostate protocol (for MRI pelvis) to better visualize the prostate gland," noted Ms. Shaw.

New MRI techniques such as multiparametric MRIs obtain

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additional sequences to help visualize the prostate gland without an endorectal coil. There are also functional imaging studies used in prostate cancer.

A bone scan has long been used in prostate cancer to assess for blastic lesions, but it is less effective at assessing lytic lesions if they present in that manner. Importantly, a CT scan is always obtained in the background of the PSMA PET to help assess for anatomic correlates.

LOCALIZED TREATMENT

There are two routes for localized disease treatment with few differences in overall survival outcomes; therefore, taking into consideration side effects and logistical factors is at the forefront of the decision-making process. Patients can pursue a radical prostatectomy with or without a pelvic lymph node dissection. The other route is definitive radiation therapy with or without androgen deprivation therapy (ADT). The duration of ADT with curative intent radiation depends on risk stratification based on Gleason score, PSA, and TNM staging. The prostate-specific antigen (PSA) nadir following definitive radiation is not always zero, but it should be quite low.

For adjuvant therapy after prostatectomy, if a patient has adverse features or lymph node involvement, external beam radiation therapy (EBRT) with or without ADT can be considered. Alternatively, close monitoring for consideration of early radiotherapy if there is detectable PSA can be an option. Salvage radiation therapy is also given in the setting of biochemical recurrence.

METASTATIC TREATMENT

The basis of systemic treatments for metastatic disease is suppressing testosterone using ADT. The goal of ADT is to achieve a testosterone level of less than 50 ng/dL, which is considered a castration level of testosterone.

"I explain to patients how we treat prostate cancer by saying we have three different buckets of treatments that we can choose from. These are chemotherapy, androgen receptor inhibitors (ARIs; abiraterone, enzalutamide, apalutamide, darolutamide), and "other" (radiopharmaceuticals such as radium-223 and Lu-177-PSMA; immune modulators such as sipuleucel-T; and targeted treatments such as PARP inhibitors). While metastatic disease is not something that we can cure, it is something that we can control for a long time with these medications," explained Ms. Deinert.

Approved luteinizing hormone-reducing hormone (LHRH) agonists include leuprolide, goserelin, and triptorelin. These are injections and come in doses that range from 1-month to 6-month injections. LHRH agonists are structurally similar to LHRH and bind to the LHRH receptor in the pituitary gland, which prevents the pituitary gland from secreting luteinizing hormone (LH). This stimulates the release of both LH and follicle-stimulating hormone (FSH). Initially, this will cause a spike in the level of testosterone, but when these medications are given continuously, a negative feedback loop occurs that results in testosterone suppression.

In addition, LHRH antagonists are available. There are two drugs approved in this category: degarelix, which is an injection, and a new oral agent called relugolix. These medications prevent LHRH from binding to the pituitary gland, which prevents the secretion of LH and FSH, and results in the suppression of testosterone.

"These medications work quickly; a patient could have castration levels of testosterone within 7 days. Therefore, if a patient has painful bone metastases or large primary tumors, they will get relief quickly when you initiate treatment with these drugs," said Ms. Deinert.

Medication Highlights

There are several nuances of prescribing these different medications along with some unique characteristics to be aware of. Figure 1 depicts the settings in which the ARIs are currently approved.

Abiraterone is the ARI that has been around the longest. There is a generic version for it making it more cost effective. However, there is a downside for patients with diabetes as it is taken with a low dose of prednisone, 5 mg twice daily. Abiraterone requires frequent monitoring. When it is first started, it can cause transaminitis, so it is important to check liver function tests and monitor electrolytes every 2 weeks for the first 3 months. If patients do not experience problems during the first 3 months, the likelihood of them experiencing transaminitis is low.

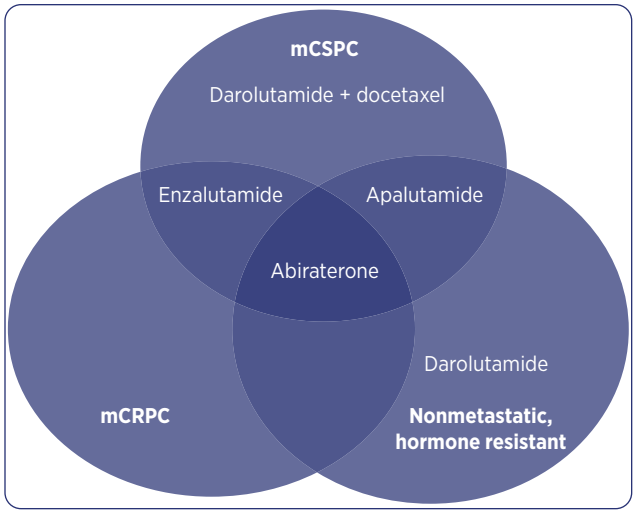

Figure 1. Androgen receptor inhibitors and their indications. mCSPC = metastatic castration-sensitive prostate cancer; mCRPC = metastatic castration-resistant prostate cancer.

Enzalutamide has a unique increased risk for seizure, which makes it contraindicated in patients with a history of seizure. It also has an interaction with clopidogrel where it can increase the toxicity of enzalutamide. If patients are on clopidogrel, then enzalutamide may need to be started at a lower dose and patients monitored closely for toxicities.

Apalutamide has a unique adverse event of rash. This maculopapular rash is oftentimes pruritic, starting in the chest and then usually spreading to the extremities or occurring in sun-exposed areas (Tohi et al., 2021). The rash usually resolves once apalutamide is stopped. However, it can be symptomatic and therefore will often be treated with topical steroids or diphenhydramine for the itching. Another unique characteristic is that it has a category X interaction with rivaroxaban where it can decrease the effectiveness of rivaroxaban and is therefore contraindicated.

The most recently approved of the ARIs is darolutamide. There have been studies that have shown that this is the best tolerated of the ARIs (Morgans et al., 2023). However, it is currently indicated in only two settings: for patients with high-volume metastatic disease in combination with docetaxel and for patients who have PSA recurrent, nonmetastatic disease that has become resistant to hormone therapy (Bayer, 2023).

The next class of drugs is immune modulators. Sipuleucel-T works by stimulating the immune response against an antigen that is expressed in the prostate cancer tissue. It is given as an infusion three times every other week and requires leukapheresis.

Another class is radiopharmaceuticals. Radium-223 is a liquid radiation that is only given for patients with bone disease. It has been shown to be well tolerated. It is an infusion that is given once a month for six doses. As a note, patients' PSA will increase while on radium-223, which will make PSA an unreliable marker during treatment. Therefore, patients will often get scans after two to three cycles and then again at the end.

A newer radiopharmaceutical agent that was approved based on data from the VISION study is Lu-177-PSMA. This is a liquid radiation that is approved for patients who have PSMA-positive disease on PET imaging and progressed on taxane based chemotherapy and an ARI. PSMA is a protein that is unique to prostate cancer cells and found on the cell membrane. It is given once every 6 weeks for six doses. Radiation precautions must be taken after receiving the treatment, including maintaining at least 3 feet of distance from others for at least 2 days.

"The most common toxicity that we have seen in practice has been myelosuppression and dry mouth, because your salivary glands have PSMA in them," noted Ms. Deinert.

The last class of drugs is PARP inhibitors: rucaparib, abiraterone plus olaparib, and abiraterone plus niraparib for *BRCA1/2*-mutated prostate cancer, and olaparib and talazoparib plus enzalutamide for homologous recombination repair (HRR) gene-mutated prostate cancer.

SIDE EFFECT MANAGEMENT

Hot flashes are a bothersome side effect for many men. Venlafaxine at 75 mg every night at bedtime can help reduce frequency and severity.

Megestrol 20 mg twice daily can also be considered, "Although you need to outweigh it with the risk for clot development and other potential side effects," said Ms. Shaw.

Gabapentin is sometimes used, and acupuncture has demonstrated benefit.

Erectile dysfunction is a life-altering side effect for men. There are many medications to consider, including tadalafil 10 mg daily as needed and

2.5 to 5 mg daily dosing, vardenafil 10 mg as needed, and sildenafil 50 to 100 mg as needed. There are other approaches, such as vacuum-assisted devices or penile implants.

Gynecomastia can also be a side effect when the testosterone is suppressed.

"It is important to do a breast exam if patients are noting differences in their breast tissue, especially for men who have *BRCA1/2* mutations who are at a higher propensity for male breast cancer," added Ms. Shaw.

Sometimes preventative radiation can be considered to prevent gynecomastia, but after about 12 months of the symptoms, the tissue tends to become more fibrotic and radiation is less effective in that setting.

Hypertension is a common side effect of many of the ARIs; therefore, advanced practitioners should monitor and manage it as appropriate.

Hypercholesterolemia is also important to assess for prior to starting ADT with continued monitoring and management as needed. "Darolutamide, the newest ARI that we're using, does have an interaction with statins," said Ms. Shaw, who explained how you might reduce the dose of the statin to reduce complications. Encouraging exercise and a well-balanced diet is also a major facet of management.

Long-term suppression of testosterone can result in developing osteopenia or osteoporosis. Dual x-ray absorptiometry scans or bone density tests should be performed at baseline and every 1 to 2 years while on ADT. If patients develop osteopenia or osteoporosis, they will often be referred back to their primary care provider to undergo management.

Monitoring vitamin D levels is also important. For bone health specifically, providers can encourage resistance training and weight-bearing activities to increase patients' bone density.

"Things shift a little bit once a patient develops castration-resistant disease with bone metastases, as our goal of treatment is to prevent skeletal-related events or fractures," said Ms. Deinert. For this subset of patients, they should be started on bone-strengthening medications, either denosumab or zoledronic acid, regardless of bone density status. These are FDA approved to be given monthly, but there has been recent literature exploring extended dosing intervals, particularly with denosumab.

"We're giving it every 12 weeks, which was just as effective, did not increase the risk for skeletal-related events, and was more convenient for patients with less financial toxicity. Therefore, our practice has transitioned to every-3-month dosing," commented Ms. Deinert. ●

Disclosure

The presenters have no relevant financial relationships to disclose.

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