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# What Is the Pharmacist's Role in Managing mHSPC Doublet and Triplet Regimens?

**Announcer:**
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**Dr. Holle:**
This session is entitled: What is the Pharmacist's Role in Managing Metastatic Hormone-Sensitive Prostate Cancer Doublet and Triplet Regimens? My name is Lisa Holly. I'm a Clinical Professor at the University of Connecticut School of Pharmacy and I take care of prostate cancer patients at UConn Health's Neag Cancer Center.

Doublet and triplet regimens for metastatic hormone-sensitive prostate cancer are the standard of care currently, with the doublet regimens, actually with all 3 of these regimens, androgen deprivation therapy is that baseline. And the doublet regimens we add a second-generation anti-hormonal therapy such as abiraterone acetate, apalutamide, or enzalutamide. And with the triplet regimens, we combine androgen deprivation therapy with docetaxel and abiraterone, or docetaxel and darolutamide. These regimens improve overall survival and delay the time to disease progression.

Evaluating for drug interactions is a really important component of these regimens. It's also important to consider food interactions. For example, abiraterone must be taken on an empty stomach. With food, it can increase significantly the concentration of the drug. And it's a variable concentration, so it's hard to assess the toxicities. There is a micronized formulation available that can be taken with or without food, and that might be an option for patients. Darolutamide must also be taken with food because its bioavailability and concentration dosing is based upon this. Whereas apalutamide and enzalutamide can be taken with or without food.

In terms of drug interactions, it's very important to assess this at baseline and when any new medications are added to the regimens. There are numerous drug interactions that can occur, and I'm not going to talk about each one of those, but I would encourage you to consider these. Some of the key points to think about are with abiraterone acetate, CYP3A4 inducers and CYP2D6 substrates, if they are taken concurrently with abiraterone, the dosing may need to be changed with abiraterone, either increase frequency or a dose reduction of the drug depending upon the interaction. With apalutamide, it doesn't usually change the concentration of apalutamide but may result in the loss of activity of the drugs that have those metabolites. With darolutamide, again, there are also many drug interactions, and it may increase the toxicity or reduce the efficacy of darolutamide. So you would try to avoid those drug interactions if possible. And with enzalutamide, there are some dose adjustments that may need to be had as well if inhibitors or inducers of CYP2C8 or 3A4 are used. In addition, I want to point out with warfarin, it's really important with enzalutamide to monitor the INR very closely when that drug is initiated.

With docetaxel, it is a 3A4 inhibitor, so we want to think about potentially the risk for increased toxicity and to monitor more closely with those drugs.

We also need to do some significant monitoring for these oral second-generation anti-hormonal therapies. This monitoring can be found in the package insert of these drugs, but also in databases as well. And I would encourage you to review those. Some of the key points

are that abiraterone acetate can cause hepatotoxicity, so close monitoring of LFTs during the first 3 months is necessary, as well as monitoring for blood pressure, hypokalemia, fluid retention, glucose levels, and signs and symptoms of adrenal insufficiency; all based upon its mechanism of action. Apalutamide has some unique side effects such as rash. It can also cause hypothyroidism and has an increased risk of falls and fractures. Darolutamide should have hepatic and renal function assessed at baseline and periodically. And enzalutamide, a complete blood count with differential and liver function test. There is a seizure risk with the second-generation anti-androgen deprivation therapy, so we need to think about that as well, and adherence for all of these orally administered drugs.

With docetaxel, it can cause myelosuppression, hepatotoxicity, renal function can be adjusted, and patients can develop hypersensitivity reactions, as well as neuropathy, diarrhea, febrile neutropenia, and fluid retention.

Some key side effects are a rash with apalutamide, which can be managed symptomatically with oral antihistamines, topical corticosteroids, and if needed oral corticosteroids, but most of the patient's rashes will resolve. Hypothyroidism with apalutamide can be replaced with thyroid replacement drugs. With docetaxel, we would want to ensure the patient receives their dexamethasone twice daily, the day before, the day of, and the day after docetaxel. And if a patient receives or experiences a hypersensitivity reaction, we would add in pre-medications. With docetaxel, febrile neutropenia can be mitigated with prophylactic pegfilgrastim or dose reductions, and neuropathy can be mitigated by dose reductions of docetaxel or considering duloxetine.

Finally, patient education is very important. There are some resources there for you for patient education handouts, and you would talk about the normal things that we would do with education but really focusing on drug and food interactions, supportive care medications, and the appropriateness of how to take these drugs with or without food.

Thank you for your attention.

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