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Expert Panel: How Does ADT Intensification for mHSPC Affect Future Therapy Options?

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Dr. Moses:
Hello, and welcome to our discussion on how does ADT intensification for metastatic hormone-sensitive prostate cancer affect future therapy options. I'm Kelvin Moses at Vanderbilt University Medical Center. And I'm pleased to be joined by Dr. Alicia Morgans at Dana Farber in Boston. Welcome.

Dr. Morgans:
Thank you so much for having me.

Dr. Moses:
So we're familiar with metastatic hormone-sensitive prostate cancer as far as men who present with disease outside of the pelvis. And recently there have been a couple of trials that have shown about treatment intensification, particularly triplet therapy, specifically the PEACE-1 and ARASENS trial. Can you give us a little bit of a overview of those as we go into our discussion?

Dr. Morgans:
Sure. So PEACE-1 and ARASENS, both built on the backbone of ADT and docetaxel that was defined in the CHAARTED and STAMPEDE trials to add either abiraterone or darolutamide in that setting, and compared it to ADT/docetaxel. In both of these trials, they found that the triplet of ADT/docetaxel and either abiraterone or darolutamide was associated with improved survival, versus ADT/docetaxel alone. So really, for chemofit patients, for patients with aggressive disease, de novo metastatic, high-volume metastatic disease, this triplet option is I think one of the ways that we're increasingly going after patients.

Dr. Moses:
Excellent. So they have a survival benefit. They have a recurrence-free survival benefit as well. But unfortunately, a lot of these men will progress with their disease. And let's say you started with triplet therapy, where would you go as far as the next steps in their management? What tests would you get? What type of treatment options do they have?

Dr. Morgans:
Well, you know, it always really depends on how they progress. If it's really a slow progressing disease, we might think about something like sipuleucel-T, which doesn't need specific testing other than to show that there's radiographic progression of disease. But for many men who have had a triplet up front, they have a more rapid progression, a more symptomatic progression in some cases, maybe visceral involvement here, because these are patients with a poorer prognosis from the get-go often who are getting triplet. And because they've had ADT and ARSI, and docetaxel chemotherapy in the metastatic hormone-sensitive setting, they then might be eligible for something like lutetium PSMA-617, or Pluvicto is its other name. And in order to give this we would need to get a PSMA PET to demonstrate the expression of PSMA on their prostate cancer cells. If they have that, then this might be an option for them.

Dr. Moses:
Yeah, excellent. And those are some exciting developments, really again in the last couple of years. So someone started doublet therapy. They're on ADT, one of the novel hormonal therapies. What is your strategy for those who progress, particularly in light of which class and medications they've been on?

Dr. Morgans:
Yeah, it's such an important question and one that we sometimes I think, get wrong. I think the first thing I'm thinking about beyond how are they progressing, is it symptomatic asymptomatic, and all of that, is to try to change mechanism of action in this setting if I can, so if they've had one of these ARSIs, we want to try to give them something else, whether it's radium or docetaxel, sipuleucel-T to try to not just switch AR signaling inhibitors is usually a goal. And there are cases where we might try for a brief time on for a patient who's, you know, very elderly, multiple comorbidities, doesn't have many treatment options, and is maybe very slowly progressing or asymptomatic. But in general, we do want to try to switch mechanism of action.

Dr. Moses:
Absolutely. That's an important thing to discuss, because maybe a lot of people aren't aware of some of the non-hormonally based therapies that are out there.

Talk about the - you mentioned this earlier, talk about the role of germline or the patient's own DNA versus somatic genetic testing, and maybe some therapies that are available, depending on what kind of genetic mutations a patient may have.

Dr. Morgans:
Absolutely. So for patients with metastatic disease, germline genetic testing is always recommended, which is, of course, the genetic alterations that the patient may have inherited, that put that individual at risk for development of the prostate cancer. We also recommend, in metastatic CRPC, at a minimum, if not in the mHSPC setting, to get somatic tumor tissue testing as well, because half of the genetic alterations that we can target are going to be germline and half are going to be identified in somatic testing. So we need to do both to really round out the picture. These may give the patient the opportunity in that first line mCRPC setting to use things like PARP inhibitors, pembrolizumab, or maybe even PARP combination therapies if they have a BRCA1 or BRCA2 alteration.

Dr. Moses:
Absolutely. And also, patients should know their family history. So if there's a strong history of prostate cancer or a strong history of breast and ovarian cancer, that may lead you to get genetic testing to determine that.

I want to thank you for the great information. I hope everyone enjoyed it and we look forward to the question-and-answer session. Thank you.

Dr. Morgans:
Thank you.

Announcer:
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