Transcript Details

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Incorporation of guideline recommendations into the frontline care of a patient with mCRPC who is naïve to both docetaxel and novel hormone therapy

Announcer:
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Dr. Srinivas:
This is CME on ReachMD, and I'm Sandy Srinivas.

Dr. Xu:
Hello, I'm Vincent Xu.

Dr. Srinivas:
Let's start our discussion by looking at a case. I want to talk about the 70-year-old patient who had a radical prostatectomy and subsequently had a biochemical relapse and had salvage radiation. Two years later, he has a biochemical recurrence and a very slow rise in PSA. He has a long PSA doubling time greater than 10 months, and we put him on intermittent androgen deprivation therapy. He had conventional scans that were negative for metastasis. He gets somatic testing of his tumor, and interestingly was found to have a PALB2 mutation. He had a PSMA scan that did reveal multiple retroperitoneal and mediastinal nodes, and he had three bone metastases in his spine. He was completely asymptomatic, and a serum testosterone was around 20.

So let's talk a little bit about what you think would be a best option for this patient. And maybe we can talk a little bit about some of the treatments that may drive our decision.

Dr. Xu:
Great. Thank you, Dr. Srinivas. I guess when I think about this patient, the first question that comes to mind is whether this is the first PSMA PET scan he's had. And if so, whether we consider this truly CRPC. PSMA PET is so much more sensitive than the conventional imaging we used to have, so I would wonder if the mediastinal nodes and bone metastases, for example, were missed on a prior conventional scan. Or if we take the benefit of the doubt and if we're calling this CRPC.

Dr. Srinivas:
I mean, I agree. Because people come in with PSMA scans now. We do offer PSMA PET scans quite readily to our patients. But I'm convinced he has CRPC because I see his PSA going up and he has castrate levels of testosterone. It's just that rather than this being a true non-metastatic CRPC, I think we have a scan that now demonstrates that he's got visible disease that we can see.

Dr. Xu:
I see. So we know from TALAPRO-2 that we now have an approval for enzalutamide plus talazoparib. And we know that this approval was in HRR mutations, and not just in BRCA 1 and 2. And so this patient would be on label for enzalutamide plus talazoparib.

One question that comes to mind is that we seem to see that for these HRR non-BRCA mutations, the response rate may be a little bit lower than what we see in BRCA 1 and 2. For example, in TALAPRO-1, the response rate among the PALB2 subset was about 25% compared to 45 to 50% for BRCA 1 and 2. Nonetheless, I think that would be an excellent option for this patient, given the overall survival benefit that was seen compared to enzalutamide in [TALAPRO-2] and that's what I would pick for this patient. Although I have to say that there's some questions that still remain, especially with now intriguing new data from ESMO for other combinations like enzalutamide and radium-223 from the PEACE-3 trial, we don't truly know which is superior.

Dr. Srinivas:
I agree. I think our options for patients with CRPC are increasing, but I think we want to give our patients all of the options so that they get the maximum benefit both in terms of PFS but obviously if there is longevity associated with the regimen, we want our patients to be able to get it. I find the HRR panel quite interesting, because I think they are all not created equally. There's definitely different levels of response based on different mutations. I was excited to see PALB2 because I think a lot of people view PALB2 as the next BRCA. So I think amongst all of the HRR, I do think PALB2 may have a higher response compared to, let's say, some of the other HRR mutations that we have. But nonetheless, I was quite excited to see the overall survival for TALAPRO-2 combining talazoparib and enzalutamide for patients with HRR. This is the only trial of the three-part combinations that we have that have a broad approval for all of HRR. And I think I'm very happy that my patient has not had a prior NHT, which again, in our practice, is going to be quite rare, given that we have moved NHTs to earlier lines. So, there aren't too many patients in my practice who have not received a prior NHT by the time they get to CRPC. In the TALAPRO-2, there was a small fraction who only had prior NHT. So I agree, it's exactly the patient population who went on TALAPRO-2, as my patient who I think would benefit from the combination.

Maybe you can briefly talk a little bit about the adverse profile that our viewers may need to pay attention as we go on this combination.

Dr. Xu:
Great. That's such a great point, because even though there's clear advantages to this combination regimen, no IVs, all pills, but the side effects are real. I think at this point we're all very familiar with the side effects of enzalutamide, including fatigue and theoretical risk of seizure in patients who have a seizure condition. We also have in the presence of patients who are getting enzalutamide monotherapy, we know that patients have quite significant gynecomastia, though that's less often seen if it's combined with ADT. When we look at talazoparib, we're really looking at the PARP type side effects, and so patients can have some decrease in blood counts, cytopenias, patients can have increased risk for infection, and some patients have fatigue as well as GI upset.

Dr. Srinivas:
Well, great points. I think with that, our time is up. We hope you found this briefcase review useful. Thank you so much for listening.

Dr. Xu:
Thank you.

Announcer:
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