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Precision in Practice—Bringing Targeted Therapy to mHSPC

Announcer:

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Dr. Taplin:

This is CE on ReachMD, and I'm Dr. Mary-Ellen Taplin. Here with me today is Dr. Scott Tagawa.

Scott, can you share with us the latest data on next-generation PARP inhibitors?

Dr. Tagawa:

So just to kind of take a step backwards, we have several different PARP inhibitors that have demonstrated benefit either alone or in combination with ARPIs for APM-resistant disease, formerly CRPC, as I said, either single agents or in combination. And we now have combinations that show benefits in the APM-sensitive situation, where we have ADT plus abiraterone with niraparib that showed a benefit in a number of different HRD genes, has FDA approval in BRCA2, and then at ASCO 2026, the TALAPRO-3 study in a slightly expanded, slightly different setting of genes showed a benefit with ADT enzalutamide and talazoparib.

So we now have kind of the nonselective PARP inhibitors that show some benefit in multiple different disease states, whether it is from the initial post-ARPI, mostly post-chemo single-agent, to the post-ADT APMR setting, where it's ARPI unaided mostly—so ARPI plus a PARP inhibitor—and now with upfront ADT in molecularly selected individuals.

We do know that there are now PARP1-selective inhibitors. There's multiple, but the 1 with the biggest amount of data that has now started phase 3 trials is saruparib, that initially had the kind of phase 1 data, a lot of different cancers, including prostate cancer, that without randomized data looked to, number 1, maybe have a cleaner toxicity profile, and also, number 2, maybe even some better efficacy, and even some responses post-nonselective PARP inhibitors, those all-comer populations.

More recently, I think most recently at ESMO 2025, there was a couple of datasets that had saruparib alone as well as saruparib combined with several different androgen receptor pathway inhibitors, really as kind of safety studies, but also that showed nice PSA and measurable responses, although when it's in combination we don't know which one it was from, but at least safety in terms of combinations.

And that drug is now in at least three phase 3 trials. And that includes for patients that are very early. So for localized disease with radiation in a couple of groups, really intensifying what we already have with ADT and abiraterone, or in a slightly less high-risk population. And then in metastatic androgen pathway modulator-naïve or sensitive disease, or formerly hormone-sensitive, looking at an

all-comer trial, also with those with HRD, so ADT, ARPI with saruparib in those settings.

So I think that the hope is that as a possibly better tolerated, possibly more potent type of an approach, we're going to see even better benefits and tolerance. There is some preclinical data for AR targeting and PARP inhibition in an unselected patient population. That being said, my bias is that I think this is probably going to have the best therapeutic index in those that are selected for having either germline or somatic HRD.

But I think the future looks very bright and interesting.

Dr. Taplin:

That's great. Well, to summarize, PARP inhibitors have been part of our prostate cancer armamentarium for quite a while now, and we've moved on from the first-generation PARP inhibitors like olaparib to a second-generation PARP inhibitor, saruparib. And the data is promising in phase 1 and phase 2, and now this drug has moved up into several phase 3 trials, including early states of the disease. So more to come on our next-generation PARP inhibitors.

This has been a great review, and thanks for listening.

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