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The Power of Timing: Therapies That Change Outcomes

Announcer:

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Dr. Tagawa:

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

We're seeing a shift towards earlier treatment intensification in localized hormone-sensitive prostate cancer. So let's break down the data. Dr. Taplin, would you review the data for intensifying ADT with AR inhibitors in localized hormone-sensitive prostate cancer?

Dr. Taplin:

Thank you, Dr. Tagawa. I'm happy to do that. The data really revolves around 2 studies, 1 an older trial, the STAMPEDE trial, and the other trial that was just presented a few days ago at ASCO 2026, the PROTEUS trial.

So in STAMPEDE there was a cohort that included men with localized high-risk—I would say very high-risk—prostate cancer, who had to meet certain criteria, including a PSA over 40, Gleason score 8 to 10, or low-volume nodal disease. And I believe in STAMPEDE they had to have 2 of those 3 criteria, and then they were eligible to be assigned to ADT—androgen deprivation therapy—and the drug abiraterone, which is given together with prednisone versus ADT. And the results of that cohort with the abiraterone was markedly positive and really changed the standard of care.

There's been some conversation in the field: if you will, if you have a patient with high-risk disease but don't quite meet those high-risk criteria. The STAMPEDE trial was done in the UK and Switzerland, and typically in the US I would say more patients get screening and somewhat unusual to have patients with PSAs over 40. So, often in my practice, I'll use those criteria but fudge them a little bit, like if they're high risk but they have a PSA of 23, not 40, and Gleason 9, for instance, or low-volume nodal disease, then I will use the ARPI regimen with ADT.

The second trial is the PROTEUS trial, which is, I would say, a novel or landmark trial that was just presented. And that was a trial done in 2,100 men, and they had very high-risk localized disease based on large part having at least an 8 to 10, but there were specific criteria to have a number of core biopsies positive, looking for more higher-volume patients. And to get into PROTEUS, if the patient had Gleason 8 tumor, like a mix of 7 and 8, like we often see, they had to have 6 positive core biopsies at minimum. So I would say the PROTEUS regimen was not for patients who had 1 or 2 cores of Gleason 8 or 9, but the more higher-volume patients.

And in that trial, there was a component of neoadjuvant and a component of adjuvant therapy around prostatectomy. So patients were

assigned to apalutamide and ADT for 6 months before and after prostatectomy, or placebo and ADT for 6 months before and after prostatectomy.

There were 2 coprimary endpoints: metastasis-free survival and the major pathologic response seen on the prostatectomy specimens. Both primary endpoints were positive. There was a 20% by conventional and PSMA imaging reduction in metastasis or death. The investigator-assessed MFS was a 26% reduction. So a positive trial, and those positive endpoints were supported by positive secondary endpoints, including event-free survival—that's any event: PSA, local recurrence, metastasis, and time to first subsequent therapy, which was nearly 3 years difference with the apalutamide ADT compared to placebo ADT.

The secondary endpoint of MFS by conventional imaging was not a positive endpoint, and that analysis suffered from very low power, from a low number of events because of the use of PSMA PET in 70% of the patients on the PROTEUS trial.

So a positive trial, and I think, Scott, we're going to have to see how the next few months roll out, if this becomes a regimen that's listed on the NCCN. But for right now what we have is the largest phase 3 trial in localized high-risk prostate cancer, the data from that, and we'll all digest it, but I think it's likely to provide another standard-of-care treatment option with those that we know exist, which is prostatectomy or androgen deprivation therapy in a longer term, usually around 2 years, with radiation.

Dr. Tagawa:

Yeah, I agree. So I'd say taken together, STAMPEDE and PROTEUS, I think that the knife, ie, surgery, and especially modern radiation are extraordinarily good for local control, but high-risk disease in all of medical oncology tends to mean micrometastatic disease. And now that we have more intensive—it's both more intense as well as more potent hormonal therapy—hopefully we can both get better control of the local tumor, but even more important, the micrometastatic disease. And that's where I think is happening in the longer term. So we'll have options for this very high-risk disease group.

So, in summary, I think we really nailed it in terms of discussing this topic of very high-risk disease. Thanks so much, and we'll see you next time.

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