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Evidence Base for First-Line Treatment Strategies for Endometrial Cancer and Delivering Guideline-Concordant Care

Episode 6

Dr. Slomovitz:
Hi, I'm Dr. Brian Slomovitz. This is CE on ReachMD. In this episode, we'll be reviewing the first-line treatment strategies for advanced or recurrent endometrial cancer. And again, it's a great pleasure to have with us today Michelle Flint and Casey Cosgrove.

Okay, we're going to talk about what is the most important advance in the treatment of endometrial cancer over the last several years. I would say it's the incorporation of immunotherapy into all patients who have endometrial cancer at somewhere along their treatment. Okay, and we learned this from the second-line. We went from the second-line earlier, right? And we did a series of four studies in the first-line setting.

Casey, take us through that, about the four studies that were done. They were all very similar.

Dr. Cosgrove:
Yeah, I think that what we're recognizing right now is immunotherapy is here to stay in endometrial cancer management, particularly for our high-risk individuals. The NRG-GY018 (KEYNOTE-868) trial and the RUBY trial both included carboplatin and paclitaxel and either pembrolizumab or dostarlimab for each one of those trials. That was all given together, and then the chemotherapy would drop off, and we would continue the immunotherapy afterwards.

And we saw benefits across the populations, both mismatch repair deficient as well as mismatch repair proficient. I think what we see, the magnitude of benefit, is obviously much more substantial in the mismatch repair deficient group, but what we were seeing is some mismatch repair proficient patients actually seem to be getting a good response as well, and a durable response as well. And I think there's a lot of exciting exploratory analysis that still has to be figured out as to who's responding and also, importantly, who's not responding.

The DUO-E trial, also examining durvalumab, was important, and also recognizing the benefit of immunotherapy in the mismatch repair deficient group. The DUO-E trial also incorporated an arm with a PARP inhibitor, so seeing if we can kind of capitalize or do better in combination, particularly in that maintenance setting.

And then the KEYNOTE-B21 trial, which included more of our, I would say, our day-to-day endometrial cancers, our curable intent endometrial cancers, once again demonstrated this benefit for the mismatch repair deficient tumors. But unlike the RUBY, the GY018 (KEYNOTE-868) trial, and DUO-E trial, we didn't see as much of a benefit for the mismatch repair proficient curable tumors.

So right now, I think that we're reconciling all this data to figure out who the right patients are for immunotherapy, when the right time to incorporate immunotherapy is, and then also looking for better opportunities to identify those individuals that may have the best responses for the immune checkpoint in addition to chemotherapy.

Dr. Slomovitz:
Michelle, it's also about a patient taking the drug. We're incorporating this concept of maintenance therapy with these drugs. In your

experience, how difficult is it to get your patients to stay on these maintenance therapies?

NP Michelle Flint:
So my experience, the patients are happy to continue on some type of therapy. Before we had IO therapy in the maintenance setting, we were giving carboplatin/paclitaxel, six cycles. And then the patients would enter surveillance.

So now, with this introduction of IO maintenance, they're continuing on treatment. They're continuing to do something to prevent their cancer from either recurring or progressing, and they are appreciative of that option.

Dr. Slomovitz:
Great. No, that's true, and they really are happy for the opportunity.

KEYNOTE-868, which is the KEYNOTE number for GY018, it's different from the other studies because it was actually statistically designed to be two separate trials. It was powered to see the difference in dMMR patient population and a statistical difference in pMMR.

The dMMRs, we know that works. Okay? Dostarlimab, pembrolizumab, atezolizumab, durvalumab. Now, in the pMMRs, this was powered to determine a difference, and it also met its statistical endpoint, showing that pembrolizumab has a statistically beneficial outcome in patients with pMMR tumors as well.

What did that lead to? It led to two FDA approvals. So they have an all-comer FDA approval for pembrolizumab, whether it's dMMR or pMMR. Now, similarly, in the RUBY trial, albeit not two separately statistically designed studies, okay, the primary objectives in the RUBY trial were to look at the ITT population and the dMMR population, but that did, too, show a benefit amongst all-comers, leading to an all-comer FDA approval in the RUBY study as well.

So that was a great review. Casey and Michelle, thanks again for your time.