Transcript Details

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Evidence Base for Treatment Strategies for Endometrial Cancer After Disease Progression and Interdisciplinary Collaboration

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Dr. Slomovitz:
Hi. This is Dr. Brian Slomovitz. This is CE on ReachMD, and again, it's my pleasure to be here today with Michelle Flint and Casey Cosgrove. Today, I'm excited about this session, changing the treatment paradigm for endometrial cancer, incorporating immunotherapy for most of our patients.

KEYNOTE-158, it's a second-line trial. It was actually tumor-agnostic. They looked at several different tumors and, in a biomarker-specific population—meaning tumors that had mismatch repair deficiency—the response rates to pembrolizumab alone were unprecedented, greater than 50%. Showing at least – now follow me – MMR-deficient patients, giving them immunotherapy, it helps in the second-line setting.

In the unselected biomarker population, it didn't work as well. So then led by the work of Vicky Makker, what they did is they combined the checkpoint inhibitor pembrolizumab with the tyrosine kinase inhibitor lenvatinib. Earlier studies showed benefit, and then they did a head-to-head study of lenvatinib/pembrolizumab versus the standard-of-care chemotherapy in the second-line setting. And they found an overall survival advantage of immunotherapy and lenvatinib.

So right there, we proved our hypothesis, right? Second-line, MMR-deficient or proficient, the role of immunotherapy.

But we need to do better. We still need to have better treatment options after chemo, after immunotherapy, and we're getting better, I think.

But let's start off with a sort of a scenario in a patient with recurrent endometrial cancer. The patient unfortunately recurred after receiving chemotherapy, after receiving immunotherapy, and it's an endometrioid grade 1 tumor, strongly positive for estrogen receptor therapy.

So Michelle, these patients are getting oral therapies, and you're helping us monitor them very closely. Can you talk a little about our patients on aromatase inhibitors and maybe some of the other active agents, mTOR inhibitors, everolimus, and CDK4/6 inhibitors?

NP Michelle Flint:
Yes, definitely. So for these patients who are candidates for hormonal agents, we likely place them on an aromatase inhibitor like letrozole, anastrozole. There's hot flashes, night sweats, some joint aching, arthralgias, some bone density loss, but they are well tolerated.

We even find that switching between aromatase inhibitors can be helpful if someone's experiencing side effects. They might tolerate one rather than the other. We often will combine everolimus, mTOR inhibitor, with an aromatase inhibitor, letrozole and see great results with that, and really a limited side effect profile with that combination, we're able to mitigate the mouth sores that patients can experience with the everolimus.

Dr. Slomovitz:
Yeah, and the other area of hormonal therapy that I'm really encouraged by is younger patients with endometrial cancer, fertility preservation. And there, one of my favorite go-to agents is the IUD, a progestin-releasing intrauterine device.

Michelle, can you talk a little bit about this, particularly, we know there's data that shows it's effective, but how tolerable is it for our patients? And what are some of your experiences in talking to our patients about that?

NP Michelle Flint:
Yeah, so the IUD is widely used for contraception. We just are able to place it here in the office. And for these patients who do desire future fertility, it's a game changer. They're able to either have their endometrial hyperplasia be reduced back to normal, or even the very low-grade endometrioid carcinoma we've had success with. So using a progesterone IUD for treatment of cancer was amazing; when I heard that the first time, I didn't believe it. And we've seen success stories.

Dr. Slomovitz:
Great. So we've talked about that some patients that are going to be amenable to hormonal therapy with advanced recurrence.

Casey, take us – I'm so excited, as you are – the ADCs, antibody-drug conjugates, how they're sort of the next wave of treatments.

Dr. Cosgrove:
Yeah, so certainly, many of these individuals that we're having the conversation about ADCs, so prior exposure to platinum, taxane, and immunotherapy. So if they have recurrence or progression on that, then we're starting to look to see whether or not they have a biomarker-directed therapy available. So my first go-to to look at is whether or not they're HER2-positive. So this is performed with immunohistochemistry to see if they're 3+, which has an FDA indication for trastuzumab deruxtecan.

The other thing that I also know is that second-line chemotherapy options for this population don't work super great, and so I think really looking at more of that precision therapy with an ADC, we're also very excited about many of our clinical trials. So for all these individuals, I'm screening for clinical trials. We have several involving different ADCs, which have different markers that are highly prevalent on endometrial cancers, that might give individuals a much better opportunity for response compared to more traditional treatments.

Dr. Slomovitz:
Talking about HER2, there's in development, TROP2 ADC, B7-H4 ADC, alpha folate receptor ADC. The future is really bright for what we do and for our patients.

So guys, thank you very much for that commentary. We're done with this session.

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