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Guideline Considerations for Immunotherapy in Primary Advanced or Recurrent Endometrial Cancer

Announcer:
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Dr. Campos:
This is CME on ReachMD, and I'm Dr. Susanna Campos.

Dr. Salani:
And I'm Dr. Ritu Salani.

Dr. Campos:
Dr. Salani. What clinical data support guideline recommendations for first-line immunotherapy-based regimens in primary, advanced, or recurrent endometrial cancer?

Dr. Salani:
Well, as you know, this has been a really exciting couple of years for endometrial cancer, particularly in the dMMR population, but we've really seen some advances in the advanced and recurrent setting. And there have been 4 pivotal trials that have looked at the addition of checkpoint inhibitors to chemotherapy. And all of these studies had a similar strategy of chemotherapy with carboplatin and paclitaxel compared to chemotherapy with the addition of a checkpoint inhibitor followed by maintenance strategies. Now, there are some key differences in the studies, including the potential role of PARP inhibitors, but I want to focus on the role of the checkpoint inhibitors.

I want to focus on 3 studies that we have label on in the United States, and that's KEYNOTE-868, or NRG-GY018, which looked at the addition of pembrolizumab; the RUBY trial, or GOG-3031/ENGOT-EN6, which looked at dostarlimab and chemotherapy; and DUO-E, which looked at durvalumab and chemotherapy. There was also the AtTEnd trial, which looked at chemotherapy with atezolizumab. And the really interesting thing is all 4 of these trials show that the addition of a checkpoint inhibitor with chemotherapy had a profound impact on both PFS in the setting of endometrial cancer in the recurrent and advanced setting. And these were patients with measurable disease. We are seeing some trends towards overall survival, though that data is still maturing and being reported, but this has been really impactful in this setting.

We're also seeing some benefit in the pMMR or mismatch proficient populations, and this is particularly in the PFS cohorts. We're still waiting for the data in longer-term follow-up, but we're seeing some trends in overall survival as well. And this has really changed the standard of care.

And so, Dr. Campos, how do you think these data are informing current NCCN Guidelines?

Dr. Campos:
Thank you. I think these have been the pivotal trials of the last 2 years. Based on the trials that you've just very nicely described, the 018,

the RUBY trial, and the DUO-E, specifically the durvalumab and chemotherapy arm, these have actually translated into making this a preferred category recommendation for first-line therapy for recurrent endometrial carcinomas. So now we have listed on the NCCN Guidelines the pembrolizumab plus carboplatin and paclitaxel, except for carcinosarcoma, because the carcinosarcoma wasn't included in 018 and it was included in RUBY. We have listed, also, dostarlimab plus carboplatin and paclitaxel. And most recently, we've added durvalumab plus carboplatin and paclitaxel, specifically only for the dMMR.

So these trials have been pivotal to changing the up-front management of patients with endometrial cancer, as well as in the recurrent setting. So know that these also are utilized for stages III to IV tumors on a Category 1 recommendations. Some other recommendations include patients that have, for example, uterine papillary serous or carcinosarcoma that are HER2/neu positive with the utilization of trastuzumab.

So they have been very, very instrumental, both for academic practices and also for community practices.

Dr. Salani:
And I think one of the key points that we're seeing is that the deficient mismatch repair group really clearly benefits from checkpoint inhibitors, and that's what the NCCN Guidelines really highlight. I think the pMMR proficient population, we're still exploring that and understanding that. And you mentioned trastuzumab, particularly for those who have HER2 expression and/or amplifications and/or p53 wild-type, where we're seeing new strategies such as selinexor.

But I think the NCCN Guidelines really provide a great overview, particularly for practitioners who may not be treating endometrial cancers on a daily basis or regular basis. I cannot overstate the role of checkpoint inhibitors with chemotherapy followed by checkpoint inhibitor maintenance strategies in those patients with deficient mismatch repair tumors. And it really is changing the landscape. We are not only seeing improved outcomes, but we probably are providing cure for many of these patients.

Dr. Campos:
Agreed. And both Dr. Salani and I serve on the NCCN uterine committee, and I think as a committee, we try to be cognizant of the data. So I think it makes for a very valuable experience and a set of guidelines that hopefully do indeed serve both academic and community practices.

Well, this has been a brief but great discussion. I hope we gave you something to think about and thank you for tuning in.

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