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# Guideline-Based, Biomarker-Directed Treatment Options in Second-Line Recurrent Endometrial Cancer

**Announcer:**
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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**Dr. Colombo:**
This is CME on ReachMD, and I'm Dr. Nicoletta Colombo.

**Dr. Campos:**
And I'm Dr. Susana Campos.

**Dr. Colombo:**
Dr. Campos, can you take us through some of the clinical data that support guideline recommendations for biomarker-directed therapies in second-line recurrent endometrial cancer?

**Dr. Campos:**
I think one of the major studies that has really influenced our practice has been the KEYNOTE-775 study. And this was a large randomized trial that looked at 2 perspectives, lenvatinib and pembrolizumab versus that of chemotherapy. And chemotherapy was the physician's choice, and in this particular case, it was either paclitaxel or doxorubicin. And there were 2 primary endpoints in the 775 study, and it was clear that lenvatinib and the pembrolizumab arm was superior to that of chemotherapy. And that has really become a standard of care as second-line therapy in patients with endometrial cancer.

I think one of the questions that now we're facing in the world of endometrial cancer, since we have all this activity of IO in the up-front setting, is where do we place this particular study, the pembrolizumab and the lenvatinib, in the context of prior IO? And I think those are studies that are going to have to materialize sooner than later.

And another element, we have the KEYNOTE-158 study. And this is a bit of an older study at this point in time, and this was really in patient populations that had a high mutational burden; they were MSI high. And in this particular setting, pembrolizumab really did a lovely job in terms of endometrial cancer. In this particular study there are about 49 patients, and the overall response rate was about 57%. So this became a staple in the management of patients that were MSI-high or tumor mutational burden-high in the management of uterine cancer. So clearly, this started to evolve the role of immunotherapy at not only a second line and then segued into that first line.

And a study that we've heard a lot about is that of the DESTINY-PanTumor02 trial. And this study was a very interesting study. These were a group of individuals that included gynecological cancers. In this case, we're talking endometrial cancer, but it also included other disciplines. Interestingly, there was only 40 patients per cohort, and patients' HER2/neu IHC was analyzed. It was also analyzed centrally, and that's actually quite important to actually take note of it. And what was clear in the endometrial cohort, that in the IHC 3+ the overall response rate was over 80% which was quite monumental.

Dr. Colombo, how are these clinical data informing the current NCCN Guidelines?

**Dr. Colombo:**
Oh, thank you. Thank you for asking. The current NCCN Guidelines for second-line treatment of recurrent endometrial cancer include a very, very long list of chemotherapy drugs, most of which can produce a response rate in the range of 10%-15%. Now, if we look at biomarker-directed therapies, which are reported under the label "useful in certain circumstances," we find lenvatinib/pembrolizumab, which is Category 1 recommendation for patients with mismatch repair proficient tumors based on the 775 trial data that you have just reported. Interestingly, the approval in Europe by EMA is for all-comers, endometrial cancer patients, regardless of mismatch repair status.

Other biomarker-directed therapies recommended in the NCCN Guidelines are pembrolizumab in the tumor mutational burden-high tumors. But also pembrolizumab, dostarlimab, avelumab, and nivolumab in MSI-high deficient mismatch repair tumors.

There is also recommendation for the use of trastuzumab deruxtecan in HER2-positive tumors with IHC 3+ and 2+ expression. And finally, larotrectinib and entrectinib are recommended for the NTRK gene fusion-positive tumors.

**Dr. Campos:**
I mean, it's clearly a very exciting time in endometrial cancer. These are actually quite pivotal studies that have really paved the way for new treatment options in patients with endometrial cancer. It's quite exciting.

**Dr. Colombo:**
I think the advent of immunotherapy has completely changed the natural history of endometrial cancer and greatly improved the prognosis of these patients.

Well, that's all the time we have today. Thank you for the great discussion, Dr. Campos. And thanks to our audience for listening.

**Announcer:**
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