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Guideline Recommendations for Biomarker-Directed Therapies in Cervical Cancer

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

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Dr. Salani:
This is CME on ReachMD, and I'm Dr. Ritu Salani.

Dr. Colombo:
And I'm Dr. Nicoletta Colombo.

Dr. Salani:
Dr. Colombo, can you take us through the clinical data that support guideline recommendations for biomarker-directed therapies in cervical cancer?

Dr. Colombo:
Thank you. Let me start with KEYNOTE-826, which was a randomized trial to assess whether the addition of pembrolizumab to chemotherapy with or without bevacizumab could improve efficacy in patients with persistent, recurrent, or metastatic cervical cancer. And this trial demonstrated a statistically significant and clinically meaningful improvement in both progression-free survival and overall survival for the pembrolizumab arm and set the new standard of care. The relative overall survival benefit in the pembrolizumab arm appeared to increase with increase in PD-L1 expression, and the hazard ratio for the PD-L1-negative population was 1, excluding this patient from the label. The recently updated OS in the PD-L1-positive population confirmed a median overall survival 28.6 months for pembro compared to 16.5 months in the placebo arm.

Now moving to the second line, tisotumab vedotin is a tissue factor-directed ADC showing prolonged overall survival compared to standard of care chemotherapy. But in the DESTINY-PanTumor02 trial, 40 patients with heavily pretreated cervical cancer achieved 50% response rate to trastuzumab deruxtecan with 75% response rate in the immunohistochemistry 3+ population.

Other promising ongoing investigation include the TROP2-directed ADC sacituzumab govitecan, which demonstrated an overall response rate of 58% in combination with pembrolizumab in previously treated cervical cancer patients.

So, Dr. Salani, now that we have reviewed some of the data, can you go more into the detail about guideline recommendation for biomarker-directed therapies for cervical cancer?

Dr. Salani:
Yeah. The studies that you kind of reviewed actually kind of indicate the NCCN Guidelines. So first-line chemotherapy with platinum-based regimen, pembrolizumab with or without bevacizumab, is Category 1 based on the data that you kind of led, which is really exciting and has really improved both progression-free and overall survival for those patients whose tumors have a CPS greater than or equal to 1.

You mentioned tisotumab vedotin, and although we don't test the biomarker, I think it's a really important strategy in the management of recurrent cervical cancer using tisotumab vedotin following frontline chemotherapy, and it continues to be used in that setting. Trastuzumab deruxtecan for the HER2-positive tumors with IHC 2+ and 3+ is on the NCCN recommendations. It's also FDA-approved for the 3+ IHC in the United States and actually has compelling responses. Although it may be a low-incidence finding in cervical cancers, it really can be a useful strategy. And I agree. I think some of these areas of exploration, including TROP2, there's some data looking at nectin-4, also provide some interesting opportunities for future patient treatment.

Dr. Colombo:
Thank you very much.

So just to sum up, I think we are really witnessing incredible advances in the treatment of advanced cervical cancer. Now, the median overall survival with cisplatin alone was 7 months, and now we can achieve up to 28 months with some of these patients experiencing long-lasting complete responses. But also the new drugs on the horizon are very promising. I mean, 75% response rate in the IHC 3+ population treated with trastuzumab deruxtecan and 58% with sacituzumab govitecan in combination with pembrolizumab is almost a dream, which, however, should be confirmed, of course, in a larger population.

Dr. Salani:
Yeah, and just to kind of piggyback on that, we do have the study being developed looking at TROP2 targets, and it will further explore the expression rate and how that impacts responses.

And I think it's also really important just to recognize that tumor testing for cervical cancer was really kind of nonexistent prior to these more recent studies, and so now doing NGS testing, IHC testing actually may inform future treatment strategies, so it's an important part of how we manage these patients.

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

Announcer:
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