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Closing the Gap: Personalized Approaches to Cervical Cancer Screening and Treatment

Announcer open:

Welcome to CME on ReachMD. This activity entitled *Closing the Gap: Personalized Approaches to Cervical Cancer Screening and Treatment* is provided by RMEI Medical Education LLC and is supported by an independent medical educational grant from Merck. Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements, as well as the learning objectives.

Dr. Salani:

Hello, I'm Dr. Ritu Salani from UCLA Health in Los Angeles, California. Today I will be focusing on several key facets related to cervical cancer screening, biomarker testing, and treatment. As part of this accredited continuing education activity, a patient experience survey was fielded to women living with cervical cancer, the results of which guide the content for this activity. In addition, the insights gleaned from this survey also informed the creation of a patient education infographic that is available to be downloaded as part of this activity.

An estimated 13,960 women will be diagnosed with invasive cervical cancer, and 4,310 will die of the disease this year in the United States. Cervical cancer is a preventable disease. We now have the availability of human papillomavirus vaccination, or HPV vaccine, and screening including cytology and high-risk HPV testing. When malignant changes are found in the cervix during screening, they can be excised before progressing to cancer. If cervical cancer is caught early, while it is localized, the 5-year survival is excellent, exceeding 90%. However, if we catch it when it is distant or metastatic disease, 5-year survival is only 19%. When we return, I will focus on the importance of guideline-based cervical cancer screening.

Welcome back. Now I would like to share a story with you about a patient named Tina who is a 38-year-old African American female. One year ago, Tina started experiencing vaginal bleeding and spotting between her menstrual cycles and after sexual intercourse. Tina was unaware that the symptoms she had could be signs of cervical cancer. Unfortunately, Tina had never been screened for cervical cancer prior. Similarly, in our patient experience survey, 64% of individuals living with cervical cancer were unaware that they needed cervical cancer screening. The US Preventative Services Taskforce has issued recommendations for routine cervical cancer screening in individuals who are not high-risk. This includes for women aged 21-29 cytology alone every 3 years, and for women ages 30-65 cytology alone every 3 years or the FDA-approved primary high-risk HPV testing every 5 years. You can also do co-testing with both of these tests every 5 years.

It's important to note that cervical cancer screening is not recommended for women after the age of 65 if they have adequate negative prior tests, or if women have had a hysterectomy with no prior history of cervical dysplasia or cervical cancer. So, the question is, should Tina have been identified previously as part of a high-risk vulnerable population and should she have been encouraged to undergo cervical cancer screening? While it is important to recognize that all women should be screened for cervical cancer, women from racial ethnic minority groups like Tina are significantly more likely to have never been screened for cervical cancer than non-Hispanic white women. Black women and Hispanic women are also more likely to be diagnosed with advanced-stage cervical cancer than white women.

Early cervical cancer is often asymptomatic, but symptoms can present and include abnormal vaginal bleeding after menopause or after sexual intercourse, periods that are long or heavier than they usually are, or unusual vaginal discharge that may include blood. Pain in

the pelvic region and pain during sexual intercourse are other symptoms that may occur. Symptoms of more advanced disease can include swelling of the legs, problems urinating, or problems having a bowel movement, and blood in the urine. Like Tina, 29% of individuals living with cervical cancer who responded to the patient experience survey were unaware of early cervical cancer symptoms prior to diagnosis.

When we return, I will continue Tina's story and dive into her diagnosis.

Welcome back. Let's return to Tina's story. As a reminder, Tina had been experiencing vaginal bleeding and spotting between menstrual periods and after sexual intercourse for the past year. In addition to the bleeding, she also noted leg swelling and problems urinating as well. After several tests for other conditions, Tina was then referred to a gynecologist. After listening to Tina's symptoms and her history, her gynecologist performed a physical examination and found a large mass on her cervix. A subsequent biopsy was done and revealed squamous cell carcinoma, positive for HPV 16. Tina's gynecologist explained that she had cervical cancer and that she would need to do imaging with a combined PET/CT scan to see if her cancer had spread. Tina was really upset to find out that this could have been caught earlier if she had been screened regularly for cervical cancer. She did undergo a PET/CT scan and it revealed additional tumors in her liver and her lungs. Based on her pathology and imaging results, Tina was diagnosed with a stage 4b cervical cancer.

In our patient experience survey, 21% responded that they were not provided with proper educational support following their cervical cancer diagnosis, and 78% felt alone when they were diagnosed. Tina's gynecologist refers her to an oncologist to start systemic treatment. Before starting treatment, what biomarkers are important to test for Tina's primary tumor?

The National Comprehensive Cancer Network Guidelines for cervical cancer recommend PD-L1 testing before first-line treatment for patients with recurrent, progressive, or metastatic disease. To help guide second-line treatment choices, they recommend mismatch or repair, or microsatellite instability testing for patients with recurrent disease, and NTRK gene fusion testing for patients with cervical sarcoma. The guidelines also recommend considering tumor mutational burden testing and Red Gene fusion testing to help determine additional treatment options.

Tina's tumor was tested for PD-L1 status and came back positive. Based on these results, and the fact that Tina has metastatic cervical cancer, what treatment should she receive?

Since her tumor is positive for PD-L1, Tina is the ideal candidate for first-line treatment with guideline preferred anti-PD-1 therapy. We will discuss her treatment options further in the next section.

Since Tina has metastatic cervical cancer, and her primary tumor is positive for PD-L1, the NCCN guidelines recommend that she receive pembrolizumab with platinum-based chemotherapy with paclitaxel with or without bevacizumab. Tina's oncologist explains the recommended regimen with bevacizumab to her, including how pembrolizumab will activate her immune system to kill the cancer cells.

Tina's oncologist also tells her about the results of a KEYNOTE 826 study. KEYNOTE 826 included patients with persistent, recurrent, or metastatic adenocarcinoma, adeno-squamous carcinoma, or squamous cell carcinoma of the cervix who had not received prior systemic therapy. Patients were randomized to receive pembrolizumab or placebo with platinum-based chemotherapy with or without bevacizumab. The addition of pembrolizumab to chemotherapy with or without bevacizumab was noted to significantly reduce the risk of death by 40% in the population with a PD-L1 combined positive score of greater than or equal to 1. This benefit of pembrolizumab plus chemotherapy was observed regardless of bevacizumab use in this study.

Tina's oncologist assures her that her survival benefit achieved by adding pembrolizumab to chemotherapy was not accompanied by a decrease in health-related quality of life. However, many patients cannot afford cervical cancer care. In our patient experience survey, 25% of respondents indicated that out-of-pocket costs for cervical cancer was unmanageable for them. In addition, when asked what barriers to medical care do you experience, and then open-ended questions, several individuals responded that the cost of treatment kept them from getting appropriate care. Other common responses to these questions included a lack of transportation, or not being able to get appointments in a timely manner due to shortages or long waiting lists.

Before starting treatment, Tina's oncologist tells her that the most common side effects that occurred in KEYNOTE 826 were anemia, neutropenia, and hypertension. Her oncologist also explains immune-related adverse events to Tina, and the most common of these in this study were thyroid disorders, colitis, severe skin reactions, and pneumonitis. Tina's oncologist instructs her to notify her oncology healthcare team if she experiences several symptoms, this includes severe fatigue or rash, several pulmonary symptoms such as cough, shortness of breath or chest pain, abdominal bloating, change in bowel patterns, weight loss, or severe muscle weakness or pain. Tina's oncologist also gives her a wallet card to carry with her at all times that states that she is receiving pembrolizumab. It also lists potential immune-related adverse events and has contact numbers for her oncology healthcare team.

Another important strategy for mitigating immune-related adverse events is obtaining laboratory tests. This should be done prior to each

treatment and at regular intervals after completing pembrolizumab to assess for organ function. Before starting treatment, and again before each additional treatment, Tina has blood drawn for laboratory tests to monitor for these adverse events and assess kidney, liver, thyroid, and pancreatic function. After receiving 3 pembrolizumab infusions, Tina starts having significant fatigue and reports being cold all of the time. Her routine bloodwork is done and reveals that her TSH is elevated. A follow-up test indicates that her T4 is also low. Both of these tests are consistent with hypothyroidism. Tina's treatment regimen is continued, but she is referred to an endocrinologist. The endocrinologist starts Tina on levothyroxine. Once the optimal dose of thyroid hormone is achieved, Tina has more energy and is no longer cold all the time.

Tina's story highlights the importance of guideline recommended cervical cancer screening to catch cervical cancer early, or more importantly before it develops, biomarker testing to guide cervical cancer treatment decisions and immunotherapeutic strategies for treatment of persistent, recurrent, or metastatic cervical cancer.

That concludes our activity for today and I hope you found it useful. Don't forget to download the infographic to help educate your patients about cervical cancer.

Announcer close:

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