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## Diversity in HER2 Expression Among Gynecologic Cancers

### 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.

In this brief lecture, I'll discuss diversity in HER2 expression among various gynecologic cancers. Here you can see HER2 expression across different tumor types, and as noted by the graph, endometrial cancer, cervical cancer, and ovarian cancer all have varying degrees of HER2 expression with the highest rate being seen in the endometrial cancer. When this was looked at recently in the PanTumor02 DESTINY trial, HER2 expression via IHC with 3+ or 2+ was reported. In general, endometrial cancer has the highest rate but it's still fairly low, ranging from 6% to 17% with IHC 3+ but an additional 13% to 39% with IHC 2+. In cervix cancer, it's about 4% to 11% that have IHC 3+ and an additional 18% who have IHC 2+. Ovarian cancer has IHC 3+ at 2% to 5% and then IHC 2+ of 8% to 18%.

Now this may vary as we start to test for IHC HER2 expression more consistently. We're also going to talk about different ways of measuring HER2 expression, which is also varied over time. The PanTumor study looked at trastuzumab deruxtecan in these tumor types and found that we can actually target HER2 overexpression in meaningful ways.

Here's an example of intratumoral heterogeneity. And this is important to recognize that tumors may have different patterns of expression in different tumor sites or even temporally, meaning at different times of the tumor's journey, so at the time of diagnosis versus time of recurrence. And here in this graph you can see specimens from the endometrial curettage with HER2 expression, but then also in the hysterectomy specimen, and it's important to recognize that repeat testing or testing of multiple areas may be meaningful.

HER2 expression in metastatic lesions versus primary tumors is a great example of that heterogeneity in tumors. We have seen discordant HER2 expression between paired and primary metastatic lesions, and you may also see a reduction in HER2 expression from the primary to metastatic tumor. So testing early may be really important, but repeat testing may also be meaningful. Loss of HER2 expression is common in metastatic endometrial cancer lesions, and as we study the other gynecologic malignancies more, we'll probably understand the expression in those tumors as well.

The tumor journey for HER2 testing has really been exciting, and I think it continues to evolve, but we've gotten a kind of a good plan thus far. At the time of diagnosis most patients have a biopsy or a surgical pathology specimen, and this is a time where HER2 testing can be the most meaningful. It's important to recognize that there's different types of HER2 testing. You can do immunohistochemistry, ELISA, Western blot, in situ hybridization, or even mutation characteristics with NGS. And so there's different methods of testing different types of HER2 mutations, amplifications, or overexpressions, and this may be important to help inform which targeted therapies

are most important.

And lastly, the different types of HER2 testing, when we look at overexpression, there are different ways of interpreting the IHC. There's breast, which has been commonly used in endometrial cancer, and now with the PanTumor02 trial, gastric testing has also come about. It's important to recognize what type of testing was done as this may actually help inform the most appropriate approach for the patient.

Well, my time is up, and I hope I've given you something to think about. Thanks so much for listening.

**Announcer:**

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