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Endometrial Cancer: HER2-Targeted ADCs: A Promising Approach to Address Unmet Needs

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

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Dr. Moore:
HER2-positive endometrial cancers have the highest risk for progression and recurrence and the lowest rates of survival among solid tumors. Is it possible for HER2 antibody-drug conjugates, or ADCs, to be successful in this space?

This is CME on ReachMD, and I'm Dr. Kathleen Moore.

Although there's been success with HER2-targeted therapies in breast and gastric cancers, we've really not seen similar benefits in patients with HER2-positive endometrial cancer until recently. HER2 antibody-drug conjugates have novel cytotoxic payloads to generate improved outcomes, and we've seen this in breast and gastric cancer.

The DESTINY-PanTumor02 study evaluated the efficacy of the HER2 antibody-drug conjugate trastuzumab deruxtecan in a variety of HER2-expressing solid tumors, inclusive of endometrial cancer. So this clinical trial was a basket study. It enrolled any solid tumor that had HER2 immunohistochemistry positivity of 2+ or 3+ by gastric scoring. They had to be recurrent and of good performance status, but otherwise could be enrolled to 1 of 7 cohorts in this basket trial, 1 of which was endometrial cancer. So there were 40 patients who were treated with trastuzumab deruxtecan at 5.4 mg/kg every 3 weeks. We saw the results of this readout at this year's ASCO, and these results have not been published as well. And they are pretty promising.

If you look at the all-comers, all 40 patients who were enrolled based on local testing, the response rate in the recurrent setting was almost 58%. And I'll remind you, the benchmark in recurrent endometrial cancer setting with our best agent, which is lenvatinib and pembrolizumab, is 33%. But now that immunotherapies have moved much into frontline, our benchmark is 15%. So this is order-of-magnitudes better. Further, if you look at those tumors that were centrally confirmed to be 3+ IHC, the response rate was 85%, and then centrally confirmed 2+ was 47% for patients with endometrial cancer.

Even though it was a single-arm study, it did report out, as just a benchmark, the median progression-free survivals, and we see here, again, just phenomenal. In the 3+ the median wasn't reached, and in the 2+ it was 8.5 months, all-comers 11 months. We don't see anything like this in endometrial cancer, so it's really quite exciting.

There were no new toxicities reported with the DESTINY-PanTumor study that we didn't already know about, and so there's common but low-grade nausea, vomiting, and fatigue. Low-grade alopecia, so you need to warn patients about that. And of course, as this becomes more broadly available, education of our providers around how to recognize interstitial lung disease when it's grade 1, not symptomatic. These nonspecific inflammatory changes can be very hard to discern from sort of things that we see just in the background, but we have to be vigilant about holding and working these up so that patients can be maintained on this medication safely.

There are other antibody-drug conjugates and targeted agents for HER2 also in the endometrial space, so it's important to remember

there's quite a lot of development here. There's BDC-1001, which is an immune-stimulating antibody-drug conjugate that is conjugated with, actually, an immune conjugate, a toll-like receptors 7/8. This is very exciting and is currently in development in endometrial cancer. ORM-5029 is another HER2 ADC. And DB-1303 is another HER2 ADC that we saw results for this year at the European Society of Gynecologic Oncology with a response rate above 50%, here with breast scoring 1+ and up.

So a lot of promising efficacy data coming out just this year, and we expect many of these agents to move into later-phase, registration-enabling studies and hopefully more broad availability for our patients. So it's an exciting time, finally, for patients with endometrial cancer.

That's all the time we have today. Thank you for joining me.

Announcer:
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