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Ovarian Cancer: Advances in HER2-Targeted ADCs

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

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Dr. Moore:
Ovarian cancer remains one of the deadliest cancers for women with a 50% 5-year survival rate. However, new data has demonstrated that HER2-targeted therapies are a potential treatment option for advanced HER2-positive tumors.

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

We have seen, and been a little jealous of, the success our colleagues are having with HER2-targeted antibody-drug conjugates in HER2-positive breast and gastric cancer. But this year, in 2023, we actually saw promising efficacy signals in ovarian cancer in the recurrent setting from the DESTINY-PanTumor02 study. This study was presented and is now published. It was a basket trial that allowed patients with all solid tumors that were HER2 expressing, but they had to be 2+ or 3+ immunohistochemistry gastric scoring for HER2. And they had to be recurrent.

And then they could have access to the DESTINY-PanTumor02 study, which allowed access to trastuzumab deruxtecan. One of the several cohorts in this study was a cohort for recurrent ovarian cancer, and so we saw early results for this 40-patient cohort that were quite promising.

When we look at the efficacy seen in the ovarian cancer cohort, when we looked at all-comers, the 40 patients who were enrolled, the response rate was 45%. Now remember, this is the recurrent setting where our benchmark for response is about 15%. This is order-of-magnitudes better. But it gets even more promising. If you look at those centrally confirmed 3+ tumors, the response rate was 64%, and then was still around 40%, or a little less than, for the centrally confirmed 2+ immunohistochemistry. So this was a very promising signal from a response rate standpoint.

Further speaking to the promising efficacy signal, when you look at the median progression-free survival, it was sitting at right about a year – 12.5 months for those tumors that were 3+ on central reconfirmation. So again, a high response rate and durable, so very exciting results for us.

From a toxicity standpoint, there were no new toxicity signals demonstrated in the DESTINY-PanTumor study that had not been previously reported, but just to quickly review, we see frequent but low-grade nausea, vomiting, so premedication is important. Low-grade fatigue. Little bit of low-grade alopecia, and so this is important to remind patients about in case they want to use cold caps. We do have to be vigilant about monitoring for development of pneumonitis or for interstitial lung disease, and so this can be these nonspecific inflammatory changes that show up on CT scans that honestly many of us didn't pay attention to for a long time. Now we have to pay attention, hold drug, and get pulmonology involved when we see those to assess whether or not this is treatment related or not. And then we also need to pay attention to ejection fraction. So pretreatment MUGA or ECHO to assure us that we have a normal

ejection fraction, and then a repeat at 3 or 4 months just to make sure we're not losing any cardiac function, with referral to cardiology when we see that.

So with these safety tips in mind, we can use, hopefully, this new class of agents in appropriately selected patients. So this is a very important development for patients with recurrent ovarian cancer. I think we'll see larger studies coming into the landscape to confirm this efficacy. We'll have to wait and hopefully get our patients enrolled there.

In addition to trastuzumab deruxtecan, there are several other antibody-drug conjugates in development also looking at ovarian cancer. For example, ORM-5029 is another HER2-targeted antibody-drug conjugate. DB-1303 is another HER2-targeting antibody-drug conjugate. They're all a little different from one another, and they're looking at a variety of solid tumors, inclusive of ovary cancer. So I think we're going to see quite a few of these agents reading out and, hopefully, more of these agents moving forward into registration-type studies for our patients.

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

Announcer:
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