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Emerging Data Evaluating HER2-Directed Therapies in Gynecologic Cancers

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

Today I'll review some emerging data evaluating HER2-directed therapies in gynecologic cancers. So let's get started.

Here is an overview of a basket trial using trastuzumab emtansine, or T-DM1, in HER2-amplified tumors, and as you can see, there are a variety of different tumors. I'm going to highlight the gynecologic malignancies here with endometrial cancer represented in that orange-yellow color and then ovarian cancer represented in the light purple.

And what this study showed is that the use of trastuzumab emtansine really kind of showed great responses in endometrial cancer. As you can see here, there was an overall objective response rate of 21%, with endometrial cancer patients really deriving some benefit, either stable disease or partial responses. Unfortunately, in ovarian cancer we didn't see a lot of responses, but there's more data that show that these patients may derive benefit from trastuzumab ADCs.

This next slide kind of focuses on that same group of patients but really looking at persistent HER2 amplification after disease progression. And one thing that was really interesting is that those patients with endometrial cancer who continue to have HER2 expression or amplification at disease progression really derived the best response. So these were patients who continued to have high levels of expression, and this is something that can be very meaningful in that the tumors are not mutating. So this is something to kind of keep our eye on as we learn more about this tumor treatment.

What really helped change the landscape for the role of trastuzumab ADCs was the phase 2 DESTINY-PanTumor02 trial, and this was also a basket trial looking at HER2-expressing solid tumors. Once again, I'm going to focus on the gynecologic cancers, and in this group, they included cervical cancer, endometrial cancer, and ovarian cancer. It's important to know that these patients were all kind of heavily pretreated for the most part and didn't really have any other real standard options of therapy. Patients were required to have IHC 3+ or 2+ by local testing and then they were centrally confirmed. Patients were treated or eligible based on the gastric scoring for HER2 expression, and you can see that the primary endpoint was confirmed objective response rate.

This data was presented and was really exciting, and here you can see the 3 tables that are highlighted, endometrial cancer, cervical cancer, and ovarian cancer, all had really profound rates. These are small numbers, and you can see that the IHC 3+ and 2+ was not 100% in each cohort because in central testing some of these dropped out. However, those who had IHC 3+ had the most pronounced objective response rates. You can see at almost 85% this time in the report in endometrial cancer, 75% in cervical cancer, and 64% in ovarian cancer, which are much higher than rates that we see compared to standard chemotherapy in this similar setting. Duration of response was about 11 months in most patients but even longer in those with IHC 3+, showing that this is kind of like a correlated target

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for this treatment.

Here's an example of a change in target lesion from baseline, and these waterfall plots are also very impressive. The green waterfall plots are the gynecologic malignancies, and you can really see that a majority of patients had stable disease or partial or complete response. And then you can also see that the duration of response, shown on the right side of the table, was also really impressive, with some patients achieving response over 2 years.

In this slide we show the PFS and OS in the gynecologic malignancies from the phase 2 DESTINY-PanTumor02 trial. These data were really exciting. In the top line you can see the progression-free survival, and across the board in the gynecologic malignancies, patients with IHC 3+ had the most pronounced response. And it's important to note that these patients were often heavily pretreated and really didn't have any therapeutic options. In the bottom portion of this table you can see the overall survival, and once again, patients with IHC 3+ derived the best benefit, although IHC 2+ also had significant gain.

And then lastly, the safety summary. With new therapies, we always need to be ready for new side effects. And once again, I'm going to focus on the gynecologic malignancies, which are the first 3 shown here. Treatment adverse-related events were common across all tumor types, and gyn cancers were no exception. And you can see that grade 3 or higher adverse events happen in about 35% to 50% of patients.

Well, this ends my time and I hope you found this review useful. Thank you for listening.

Announcer:
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