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Leveraging Clinical Data: HER2-Targeted ADCs in Second-Line and Beyond MBC

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

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Dr. Anders:
Welcome to CME on ReachMD. My name is Dr. Carey Anders, and today, I will be reviewing the very clinically relevant data from the pooled analysis of DESTINY-Breast01, 02, and 03, as well as the DESTINY-Breast12 study. These studies effectively are evaluating the antibody-drug conjugate trastuzumab deruxtecan for patients with HER2-positive breast cancer that's metastatic to the brain.

The first analysis we'll review is the pooled analysis from three studies: DESTINEY-Breast01, 02, and 03, where they actually pooled out the proportion of patients that had brain metastasis that were asymptomatic, and treated with local therapy as patients were eligible for each of these studies in that setting.

Effectively, patients were treated with trastuzumab deruxtecan, also known as T-DXd, either as a single arm in DESTINEY-Breast01, randomized 2:1 in DESTINY-Breast02, where patients received either T-DXd or physician's choice of either trastuzumab/capecitabine or lapatinib with capecitabine. And then finally, in DESTINY-Breast03, patients received either T-DXd or TDM1 in a 1:1 fashion.

And when the investigators, led by Dr. Sara Hurvitz, looked at the best percent change in brain metastasis, they did see a clear improvement in overall response rate for patients who received the T-DXd arm compared to the comparator arms that were pooled together from TDM1, trastuzumab/capecitabine, or lapatinib/capecitabine. And, interestingly, we did see many patients who had a complete response intracranially to T-DXd.

And this did correspond with an improvement in time to next CNS event or CNS PFS. In the patients with treated or stable brain metastasis they had a CNS PFS of approximately 1 year compared to a little less than 9 months in the comparator arm. And then, interestingly, in the untreated or also deemed active brain metastasis, the difference was quite profound. Patients in the T-DXd arm had a CNS PFS of almost a year and a half at 18.5 months and the comparator 4 months. So, a pretty significant separation of the curve.

So, I think what this tells us is that from these pooled analyses, patients with HER2-positive breast cancer and brain metastasis will experience a very significant response to T-DXd that can very likely be durable.

And sort of expanding on this data, there was a prospective phase 3 before study of T-DXd in HER2-positive metastatic breast cancer. This included an arm with base-line brain metastasis and an arm without base-line brain metastasis. This is known as the DESTINY-Breast12 study. All patients in this study received T-DXd at standard dosing.

And what we found from this analysis was that the outcomes for both CNS and non-CNS patients were quite similar. The overall response rate for all patients was 64%, and the CNS overall response rate was 71%. So, even a little more robust. And then, when the investigators, led by Dr. Nancy Lynn and colleagues, looked at the 12-month overall survival rates, they found that both patients with brain metastasis and without brain metastasis had a 90% 12-month overall survival rate.

And then, finally, just in thinking about this compound in practice, we do watch for myelosuppression, nausea, fatigue. We can see alopecia. And then, I think the most unique treatment-related adverse event is interstitial lung disease or pneumonitis. And, interestingly, one difference that we did see, albeit quite small, between the patients with brain metastasis and without brain metastasis were interstitial lung disease is that the rates were a little higher in the patients with brain metastasis: 16% versus 12.9% in patients without brain metastases.

We don't really know why this is occurring. But it could be related to the fact that patients with brain metastasis are also on dexamethasone, and that may make them at higher risk for opportunistic infection. So, always important to think about prophylaxis in that patient population or infections such as PJP pneumonia.

So, I think this collective data really does illustrate that T-DXd is a fantastic option for our patients with HER2-positive breast cancer brain metastasis. And I thank you for your attention.

Announcer:
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