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Which TNBC Patients Are Eligible for ADCs?

Announcer:
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Dr. Hurvitz:
Hi there. I'm Dr. Sara Horvitz from UCLA, and I'm going to be talking about which patients with triple-negative breast cancer are eligible for antibody drug conjugates.

There was a large phase 3 clinical trial called ASCENT that evaluated the use of sacituzumab, an ADC that targets TROP2 in triple-negative metastatic breast cancer. Data from this study ultimately led to the regulatory approval of this agent in this setting. To be eligible to go on this clinical trial, patients had to have triple-negative breast cancer and have received at least two prior lines of chemotherapy and there was no upper limit of prior lines of chemotherapy. One line of chemo could include progression of disease within 12 months of chemotherapy in the adjuvant or neoadjuvant setting. Patients had to have had a prior taxane for the purposes of this study, had to have measurable disease, and a good performance status. And they were allowed on if they had brain metastases, as long as those brain metastases were stable for at least 4 weeks prior to treatment on study. All patients in this study, as I mentioned, had triple-negative breast cancer.

The results from the trial demonstrated a very important statistically significant and clinically meaningful improvement in the progression-free survival and overall survival with the use of sacituzumab govitecan compared to single-agent chemotherapy, and interestingly, those benefits were seen regardless of age of patients, race, prior type of treatments that were received, the region, whether or not the patient's tumors were PD-L1 positive or negative, or the location of their disease in their body.

There was an analysis also done to see whether this drug was useful in patients based on tumor TROP2 expression level. And interestingly, patients with varying degrees of TROP2 expression still received benefit from sacituzumab compared to chemotherapy. They derived this benefit regardless of level of TROP2 expression.

And it's notable that TROP2 expression is relatively ubiquitous across triple-negative breast cancers. Patients also derive benefit regardless of whether or not they were carriers of a BRCA mutation.

Another ADC that's available for triple-negative breast cancer is trastuzumab deruxtecan which was evaluated in the DESTINY-Breast04 clinical trial, looking at patients with HER2-low expression but non-HER2-amplified breast cancer. About 10% of patients in this trial had triple-negative, HER2-low-expressing breast cancers. And they were allowed if they'd had one to two prior lines of chemotherapy in the metastatic setting. And those patients with treated stable brain metastases were allowed on study.

In this clinical trial, the exploratory analysis of PFS and OS for those patients with triple-negative disease demonstrated a significant improvement in PFS and OS. The data are ,of course, limited by the low patient numbers, only 10% of the patients in this trial had triple-negative disease. But this drug is available for patients with triple-negative HER2-low-expressing breast cancer, making it the second ADC available for triple-negative metastatic disease.

The benefits with T-DXd in patients with ER expression of 0% versus 1 to 10% also appeared to be quite good. There didn't appear to be much of a difference based on low levels of ER expression or no ER expression.

So one thing that clinicians I think must grapple with is choosing between these two ADCs for triple-negative breast cancer. They had similar inclusion criteria for the clinical trials. The ASCENT study required at least two prior chemotherapies in the metastatic setting, whereas the DESTINY-Breast04 study required only one prior line of chemo in the metastatic setting. That said, the ASCENT study was entirely evaluating triple-negative breast cancer patients, whereas the DESTINY-Breast04 only included 10% of patients having triple-negative disease in the overall study.

One might use the toxicity profile to decide between these two agents in patients who have HER2-low-expressing metastatic breast cancer. If a patient has underlying interstitial lung disease, one would probably not choose T-DXd, and if a patient had significant risks for febrile neutropenia, sacituzumab may not be the ideal agent.

Thank you.

Announcer:
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