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Who Is the Best Candidate for Sequencing Sacituzumab Govitecan Before T-DXd in HR+ Breast Cancer?

Announcer:
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Dr. Sammons:
Hello, my name is Dr. Sarah Sammons, and I'm Associate Director of the Metastatic Breast Cancer Program at Dana Farber Cancer Institute in Boston, Massachusetts. Thank you so much for joining me today about this intriguing topic on who is the best candidate for sequencing sacituzumab govitecan before T-DXd in hormone receptor-positive breast cancer.We will first start with a case of a 49-year-old female with metastatic hormone receptor-positive HER2-0 breast cancer. She was diagnosed in 2019 with de novo metastatic breast cancer with bone metastasis. She had original next generation sequencing which showed that her tumor molecular burden was low. She had no ESR1 or PI3 kinase mutation. She was BRCA negative and her HER2 status by immunohistochemistry was 0. She was treated in the first line with palbociclib, letrozole, and zoledronic acid for her bone metastasis. Two years later, in 2021, she had progressed with two new liver lesions after 22 months of therapy. She was placed on second-line everolimus and exemestane, of which 4 months later she had progression in the liver. At this time, she was placed on third-line capecitabine, and after 6 months she had progression in the liver and bone. A repeat biopsy of her liver metastasis showed that she was still HER2-0 by immunohistochemistry. And she was treated with fourth-line paclitaxel. She now has progressive disease after 5 months of paclitaxel.

What next line of therapy would you choose? One, trastuzumab deruxtecan; 2, sacituzumab govitecan; 3, liposomal doxorubicin; or 4, eribulin. For review, sacituzumab govitecan is the first FDA approved TROP2 antibody drug conjugate approved in both triple-negative and hormone receptor-positive breast cancer.

Based on the TROPiCS-02 phase 3 clinical trial sacituzumab was studied versus physician's choice chemotherapy in over 500 patients with metastatic breast cancer. All patients, like this patient, in the current study had prior CDK4/6 inhibitors and a median of 3 prior lines of chemotherapy. Sacituzumab govitecan improved progression-free survival and overall survival versus physician's choice chemotherapy, and was statistically significant. Antibody drug conjugates have redefined our treatment algorithms for hormone receptor-positive breast cancer.

The way I think about ADC is in sequencing, is split into whether or not patients are HER2-low or HER2-0. Regardless of the HER2 status in hormone receptor-positive breast cancer, we should exhaust all endocrine treatment strategies. First-line chemotherapy for both patients subsets continues to be standard-of-care systemic chemotherapy prior to antibody drug conjugate challenge. My preferred choice is capecitabine, as it is oral and generally well tolerated. After first-line capecitabine, then the HER2 status becomes important. For HER2-low patients, I generally consider after 1 line of chemotherapy, trastuzumab deruxtecan based on the results of the DESTINY-Breast04 clinical trial. For HER2-0 patients, I will often give a second line of chemotherapy such as a taxane, and this would be followed by sacituzumab, based on the results of the TROPiCS-02 clinical trial.

What patients should we sequence sacituzumab govitecan before T-DXd? Sacituzumab should be used after endocrine resistance is

established and at least 2 lines of chemotherapy have been exhausted. Sacituzumab can be considered as the first ADC in HER2-0 patients, or in HER2-low patients that have toxicity concerns for T-DXd, such as the history of interstitial lung disease or cardiac history.

Thank you so much for joining me today to understand which patients may be sequenced with sacituzumab prior to trastuzumab deruxtecan.

Announcer:
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