Transcript Details
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DESTINY-Breast11 and Neoadjuvant Care in HER2-Positive Breast Cancer

Announcer Intro:
You're listening to *On the Frontlines of Metastatic Breast Cancer* on ReachMD. Today, we'll hear from Dr. Jules Cohen, who's a Clinical Associate Professor of Medicine at Stonybrook Cancer Center in New York. He'll be discussing the DESTINY-Breast11 trial, which assessed trastuzumab deruxtecan, or T-DXd, in high-risk patients with HER2-positive, early-stage breast cancer.

Let's hear from Dr. Cohen now.

Dr. Cohen:
The DESTINY-Breast11 trial attempted to demonstrate that we could do better with pathological complete response by upgrading our neoadjuvant chemotherapy and HER2-targeted therapy. And, importantly, also, even if we could only have similar results in terms of pathological complete response rate, perhaps we could do it with less toxicity. And so the D-B11 trial, again, was a neoadjuvant trial for high-risk patients with HER2-positive, early-stage breast cancer. It was a phase III trial, open label, and the eligibility included patients with high-risk HER2-positive disease that were defined as either having at least T3 clinical disease, which were tumors greater than five centimeters, and/or patients with node-positive disease that was either seen on physical exam or on imaging.

Nine hundred and twenty-seven patients were enrolled, and they were randomized to one of three arms. The first arm was T-DXd given every three weeks at the standard dosing times four doses, followed by paclitaxel, trastuzumab and pertuzumab, which we abbreviate as THP. And that was over 12 weeks. It was compared to the standard of care in this setting, which is the dose-dense Adriamycin-cyclophosphamide therapy, given every two weeks for four doses with growth factor support, followed by THP, just like the THP in the first arm of the trial. And then finally, the third arm was a pure T-DXd monotherapy arm given every three weeks for eight doses.

Now, the T-DXd monotherapy did not perform as well as the standard of care, and that arm of the trial was closed early because there was what seemed to be a decreased rate of pathologic complete response. However, the T-DXd-THP hybrid regimen—again, four cycles of T-DXd followed by four cycles of THP—did do well and was comparable to dosed as AC followed by THP and with less toxicity. So, specifically, the primary endpoint was pathologic complete response, and the pathologic complete response rate in the T-DXd arm was 67.3 percent versus 56.3 percent in the standard-of-care arm. The delta here was 11 percent, and the p-value was highly statistically significant.

Of note, the toxicity with the hybrid arm—T-DXd followed by THP—was less than the standard of care, so the Adriamycin-cyclophosphamide standard-of-care arm was actually more toxic than the T-DXd hybrid arm. Grade 3 side effects were 37.5 percent in the T-DXd arm versus 55.8 percent in the standard-of-care arm, and serious adverse events were much more common with the Adriamycin-cyclophosphamide arm—20 percent versus 10 percent. LV dysfunction was rare in the T-DXd patients and 6.9 percent in the AC patients, and there was less myelosuppression with T-DXd. And most importantly, the interstitial lung disease was more or less the same between the two arms of the trial. The T-DXd hybrid arm had an interstitial lung disease rate of 4.4 percent, versus the Adriamycin-cyclophosphamide arm had an interstitial lung disease rate of 5.1 percent.

Announcer:
That was Dr. Jules Cohen discussing DESTINY-Breast11 and its findings on trastuzumab deruxtecan. To access this and other episodes in our series, visit *On the Frontlines of Metastatic Breast Cancer* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!