T-DXd yields superior outcomes over chemotherapy-based regimens in patients previously treated with T-DM1

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Compared with capecitabine-based regimens, trastuzumab deruxtecan (T-DXd) led to higher response rates and longer survival in the third-line setting for patients with HER2-positive metastatic breast cancer previously treated with trastuzumab emtansine (T-DM1), according to results from the phase III DESTINY-Breast02 trial presented at the San Antonio Breast Cancer Symposium, held December 6-10, 2022.

T-DXd is an antibody-drug conjugate that uses the HER2-targeted antibody trastuzumab to deliver a cytotoxic payload selectively to HER2-expressing cells. In the single-arm DESTINY-Breast01 phase II clinical trial, T-DXd showed clinical activity in the third-line setting for patients with HER2-positive metastatic breast cancer who were previously treated with T-DM1, another HER2-targeted antibody-drug conjugate.

These results led to the accelerated approval of T-DXd in 2019 as a third-line therapy for patients with metastatic or unresectable breast cancer who have received two or more prior HER2-targeted therapies.

"While DESTINY-Breast01 established T-DXd as a new treatment for this population, it was a modestly sized, single-arm phase II trial," said Ian Krop, MD, Ph.D., associate cancer center director for Clinical Research and the chief clinical research officer at the Yale Cancer Center. The DESTINY-Breast02 trial was designed as a confirmatory study for DESTINY-Breast01 to evaluate T-DXd versus treatment of physician's choice (TPC) in patients previously treated with T-DM1, he explained.

"In addition to confirming the favorable benefit-to-risk profile of T-DXd in this population, this research was also important to evaluate the efficacy of one antibody-drug conjugate, T-DXd, in patients whose cancer has already progressed on another antibody-drug conjugate, T-DM1," Krop noted. "This is the first randomized trial to ask this

important question."

The DESTINY-Breast02 trial enrolled 608 patients whose metastatic breast cancers had progressed on or after T-DM1 treatment. Patients were randomly assigned 2:1 to receive either T-DXd or TPC (a combination of capecitabine with either trastuzumab or lapatinib).

Among the patients treated with T-DXd, 69.7 percent experienced an objective response, as compared with 29.2 percent of patients treated with TPC. Those treated with T-DXd were also 64 percent less likely to experience disease progression than patients receiving TPC, with a median progression-free survival of 17.8 months and 6.9 months for patients in the T-DXd and TPC arms, respectively. Overall survival was also significantly longer for patients treated with T-DXd (39.2 months with T-DXd vs. 26.5 months with TPC).

Krop noted that adverse events in patients who received T-DXd were consistent with prior studies. T-DXd-related interstitial lung disease was observed in 10.4 percent of patients who received the therapy; most of these cases were grade 1 or 2, but two cases of grade 5 interstitial lung disease were reported.

"The results of DESTINY-Breast02 confirm the findings of DESTINY-Breast01, demonstrating high levels of efficacy of T-DXd in patients with HER2-positive metastatic breast cancer previously treated with T-DM1," said Krop. "Furthermore, they extend these findings, demonstrating that T-DXd is not only highly active, but also superior to conventional chemotherapy-based regimens in this patient population."

Follow-up analyses may assess patient-reported outcomes from this trial, and additional studies may examine adverse events, efficacy, and safety of the treatment in patients with metastases to the central nervous system, Krop noted. Ongoing studies are also evaluating T-DXd as a first-

line therapy for patients with HER2-positive metastatic breast cancer and for patients with early-stage disease.

A limitation of this study was that the control arm was limited to therapies based on capecitabine, precluding direct comparison of T-DXd to treatment regimens containing other chemotherapeutic agents. An additional limitation is that patients with progressive metastases to the central nervous system were not eligible for the trial.

More information: Conference: www.sabcs.org/

Trial info: www.clinicaltrials.gov/ct2/show/NCT03523585

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