Enhertu Shows Promise for Several Types of HER2-Positive Cancer

Response rates ranged from 56% to 85% for several types of tumors with high HER2 expression.

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The antibody-drug conjugate Enhertu (trastuzumab deruxtecan), which is currently approved for advanced breast, lung and stomach cancer, is also effective for people with several other types of tumors that express HER2, according to research presented at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting.

In the Phase II DESTINY-PanTumor02 study, overall response rates were 45% for ovarian cancer, 50% for cervical cancer and 58% for endometrial but only reached 4% for hard-to-treat pancreatic cancer. Rates were higher for tumors with stronger HER2 expression. A related study saw a 38% response rate for advanced colorectal cancer.

“HER2 is present in many cancer types, such as breast, gastric, lung, gynecologic and urothelial cancers, and patients with HER2-expressing, hard-to-treat cancers need new treatment options,” lead investigator Funda Meric-Bernstam, MD, of the University of Texas MD Anderson Cancer Center, said in an ASCO press release.

“These results advance our clinical understanding of HER2 expression, reaffirm HER2 as an actionable biomarker across a broad range of tumor types and show that trastuzumab deruxtecan could potentially provide a new treatment option for patients with advanced disease across these tumors.”

Enhertu, from Daiichi Sankyo and AstraZeneca, is an antibody-drug conjugate, a new type of treatment that uses antibodies to deliver toxic chemotherapy drugs directly to tumors. Enhertu combines the monoclonal antibody trastuzumab (Herceptin), which targets HER2, with a topoisomerase inhibitor as a payload. Tumors that strongly express HER2—a receptor for a protein that promotes cell growth—are classified as HER2-positive.

The Food and Drug Administration initially granted accelerated approval of Enhertu for the treatment of inoperable or metastatic HER2-positive breast cancer in 2019. At last year’s ASCO meeting, researchers reported that Enhertu also works well for breast tumors with low HER2 expression, leading to approval for that indication and expanding the eligible patient population. Enhertu is also approved for HER2-positive non-small-cell lung cancer and gastric or

gastroesophageal junction cancer. This suggests that people with other types of HER2-expressing tumors could benefit as well.

The open-label DESTINY-PanTumor02 trial (NCT04482309) enrolled 267 previously treated patients with HER2-expressing locally advanced or metastatic biliary tract, bladder (urothelial), cervical, endometrial, ovarian, pancreatic or other tumors. They either had progressed after at least one systemic treatment or had no available treatment options. Seventy-five patients had tumors classified as IHC 3+ (high HER2 expression), while 125 were classified as IHC 2+ (moderate HER2 expression). The participants received Enhertu at a dose of 5.4 milligrams per kilogram by intravenous infusion every three weeks.

After a median follow-up period of 9.7 months, objective response rates, indicating tumor shrinkage or remission, varied widely across cancer types and were generally better for tumors with higher HER2 expression:

- Endometrial cancer: 58% overall, 85% for IHC 3+, 47% for IHC 2+
- Cervical cancer: 50% overall, 75% for IHC 3+, 40% for IHC 2+
- Ovarian cancer: 45% overall, 63% for IHC 3+, 37% for IHC 2+
- Bladder cancer: 39% overall, 56% for IHC 3+, 35% for IHC 2+
- Biliary tract cancer: 22% overall, 56% for IHC 3+, 0% for IHC 2+
- Pancreatic cancer: 4% overall, 0% for IHC 3+, 5% for IHC 2+
- Other tumor types: 30% overall, 44% for IHC 3+, 19% for IHC 2+.

Across all tumor types, the median duration of response was 11.8 months, rising to 22.1 months for people with IHC 3+ tumors.

In a related presentation, researchers reported results from the Phase II DESTINY-CRC02 trial (NCT04744831), showing an overall response rate of 38% for people with locally advanced or metastatic colorectal cancer who were treated with the optimal 5.4 mg/kg dose. Here, too, the response rate was higher for patients with IHC 3+ tumors (47%) versus IHC 2+ tumors (6%). The median duration of response was 5.5 months, the median progression-free survival time was 5.8 months and the median overall survival time was 13.4 months.

Treatment with Enhertu was generally safe, though side effects were common. The most frequently reported severe (Grade 3 or higher) treatment-related adverse events in DESTINY PanTumor02 were white blood cell deficiency (19%), anemia (9%), fatigue (6%) and platelet deficiency (5%). Twenty people (8%) developed treatment-related interstitial lung disease or pneumonitis (lung inflammation). About 12% of participants stopped treatment due to side effects.

“This study provides data for an unmet need for patients who have exhausted standard

therapeutic options with tumors that overexpress HER2 for which no drug is yet approved," said ASCO expert Bradley McGregor, MD, of the Dana-Farber Cancer Institute. "While additional follow-up is needed, there is robust activity across multiple HER2-expressing tumors with over 50% response rate in those with the highest levels of HER2 expression coupled with an encouraging safety profile. Trastuzumab deruxtecan could provide a new treatment option for these patients."

Click here to ready the DESTINY-PanTumor02 and DESTINY-CRC02 study abstracts.
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