FDA Approves Datroway for HER2-Negative Metastatic Breast Cancer

The new antibody-drug conjugate reduced the risk of disease progression or death by 37%.

January 23, 2025 By Liz Highleyman

On January 17, the Food and Drug Administration (FDA) approved Datroway (datopotamab deruxtecan, or Dato-DXd) for people with previously treated inoperable or metastatic hormone receptor-positive/HER2-negative breast cancer. The new targeted therapy significantly reduced the risk of disease progression or death in a Phase III trial, though it did not improve overall survival.

Datroway, from AstraZeneca and Daiichi Sankyo, is a novel antibody-drug conjugate. It consists of an antibody that targets TROP-2 and delivers a topoisomerase inhibitor chemotherapy payload directly to cancer cells. This is the first FDA approval for Datroway, which is also being tested for other malignancies, including non-small-cell lung cancer.

Breast cancer is classified by the type of receptors on tumors. Most have estrogen or progesterone receptors that allow them to be treated with hormone (endocrine) therapy, classified as HR-positive. HER2-negative tumors lack a receptor for a protein that promotes cell growth and can't be treated with HER2 inhibitors such as Herceptin (trastuzumab). About 70% of breast cancer cases were traditionally classified as HR-positive/HER2-negative, though some of these are now considered HER2-low or ultralow. Triple-negative breast cancer doesn't express any of these receptors and is harder to treat.

"Despite considerable progress in the HR-positive, HER2-negative metastatic breast cancer treatment landscape, new therapies are still needed to tackle the frequent and complex challenge of disease progression after endocrine and initial chemotherapy," principal investigator Aditya Bardia, MD, MPH, of UCLA Health Jonsson Comprehensive Cancer Center, said in a news release. The approval of Datroway "marks a major therapeutic milestone and provides patients with metastatic breast cancer a new treatment alternative to conventional chemotherapy."

The approval of Datroway is supported by findings from the TROPION-Breast01 study (NCT05104866), an international clinical trial that enrolled 732 people with HR-positive/HER2-negative breast cancer who experienced disease progression or were ineligible for further endocrine therapy and who had received at least one line of prior chemotherapy for unresectable

or metastatic disease. Almost all were women, nearly half were white, about 40% were Asian, and the median age was approximately 55 years. Patients with active brain metastasis were excluded.

Participants in this open-label study were randomly assigned to receive Datroway or the investigator's choice of chemotherapy (eribulin, capecitabine, vinorelbine or gemcitabine). Datroway is administered by IV infusion once every three weeks until patients experience disease progression or unacceptable side effects.

Progression-free survival, meaning patients were still alive without worsening disease, was significantly longer in the Datroway group compared with the chemotherapy group (median 6.9 versus 4.9 months). However, overall survival was similar in both groups (18.6 versus 18.3 months). Objective response rates, indicating tumor shrinkage, were 36% and 23%, respectively. Study results were recently published in the Journal of Clinical Oncology.

Treatment with Datroway is generally safe, though side effects are common. The most frequent adverse effects include mouth sores (stomatitis), nausea and vomiting, constipation, fatigue, hair loss, eye problems, decreased white blood cell counts, decreased hemoglobin (anemia) and elevated liver enzymes. The prescribing information includes a warning about lung inflammation. Datroway can cause fetal harm if used during pregnancy.

"Only one in three patients with metastatic HR-positive, HER2-negative breast cancer live more than five years following diagnosis, highlighting the urgent need for additional effective therapies," said Caitlin Lewis of Living Beyond Breast Cancer. "The approval of Datroway is a significant advance, offering patients with metastatic HR-positive breast cancer a new and much-needed treatment option."

While TROPION-Breast01 participants were classified as HER2-negative, they had HER2 immunohistochemistry scores 0, +1 or +2, meaning some of them would now be considered HER2-low or ultralow. Another AstraZeneca/Daiichi Sankyo antibody-drug conjugate, Enhertu (fam-trastuzumab deruxtecan)—which consists of a different antibody carrying the same chemotherapy payload—was initially approved for HER2-positive metastatic breast cancer, but a recent study showed that it also works for people with HER2 low and ultralow tumors.

Datroway is also being evaluated for people with hard-to-treat triple-negative breast cancer, either alone or in combination with checkpoint inhibitor immunotherapy (TROPION-Breast02, TROPION-Breast03, TROPION-Breast04 and TROPION-Breast05).

Click here for full prescribing information for Datroway.
Click here for more news about breast cancer.

Click here for a Cancer Health feature on antibody-drug conjugates.

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