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IN BRIEF

An Expanded Indication for *Enhertu*

Fam-trastuzumab deruxtecan (*Enhertu* – Daiichi Sankyo/AstraZeneca) has now been approved by the FDA for use in combination with pertuzumab (*Perjeta*) for first-line treatment of HER2-positive unresectable or metastatic breast cancer. The drug was approved earlier for use as monotherapy in adults with previously treated HER2-positive unresectable or metastatic breast cancer.¹

STANDARD TREATMENT – HER2, a transmembrane receptor protein involved in normal cell growth, is overexpressed in about 20% of breast cancers. Amplification and/or overexpression of HER2 is associated with more aggressive disease and reduced survival. Standard first-line treatment of HER2-positive advanced or metastatic breast cancer has been a taxane plus the anti-HER2 monoclonal antibodies trastuzumab (*Herceptin*) and pertuzumab. Fam-trastuzumab deruxtecan monotherapy has been a preferred second-line option.^{2,3}

CLINICAL STUDIES – FDA approval of fam-trastuzumab deruxtecan for first-line treatment was based on the results of a randomized trial (DESTINY-Breast09) in 1157 patients with HER2-positive advanced or metastatic breast cancer who had not received chemotherapy or HER2-targeted therapy (or had received neoadjuvant or adjuvant HER2-targeted therapy more than 6 months before the diagnosis of advanced or metastatic disease). Patients were randomized to receive fam-trastuzumab deruxtecan alone, fam-trastuzumab deruxtecan plus pertuzumab, or standard treatment (a taxane, trastuzumab, and pertuzumab) until disease progression or unacceptable toxicity occurred. In the prespecified interim analysis, median progression-free survival (PFS) was significantly longer with fam-trastuzumab deruxtecan plus pertuzumab than with standard treatment (40.7 vs 26.9 months). Compared to standard treatment, patients receiving fam-trastuzumab plus pertuzumab also had a higher response rate (85.1% vs 78.6%) and a longer median duration of response (39.2 vs 26.4 months).⁴

DOSAGE, ADMINISTRATION, AND COST – The recommended dosage of *Enhertu* for first-line treatment of HER2-positive unresectable or metastatic breast cancer is 5.4 mg/kg administered intravenously once every 3 weeks in addition to pertuzumab until disease progression or unacceptable toxicity occurs. The label recommends dosage adjustments that should be made if adverse effects occur. One dose of *Enhertu* for a 70-kg patient costs about \$13,000.⁵

CONCLUSION – In one clinical trial in adults with HER2-positive unresectable or metastatic breast cancer who had not received chemotherapy or HER2-targeted therapy for advanced or metastatic disease, progression-free survival was significantly longer with fam-trastuzumab deruxtecan (*Enhertu*) plus pertuzumab (*Perjeta*) than with the current standard of care. Fam-trastuzumab deruxtecan plus pertuzumab will likely become the standard first-line treatment for HER2-positive unresectable or metastatic breast cancer. ■

1. In brief: Fam-trastuzumab deruxtecan (*Enhertu*) for breast cancer. *Med Lett Drugs Ther* 2023; 65:e60.
2. SH Giordano et al. Systemic therapy for advanced human epidermal growth factor receptor 2-positive breast cancer: ASCO guideline update. *J Clin Oncol* 2022; 40:2612.
3. F Cardoso et al. 6th and 7th international consensus guidelines for the management of advanced breast cancer (ABC guidelines 6 and 7). *Breast* 2024; 76:103756.
4. SM Tolaney et al. Trastuzumab deruxtecan plus pertuzumab for HER2-positive metastatic breast cancer. *N Engl J Med* 2026; 394:551.
5. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. May 5, 2026. Reprinted with permission by First Databank, Inc. All rights reserved. ©2026. www.fdbhealth.com/drug-pricing-policy.

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