Enhertu® (fam-trastuzumab deruxtecan-nxki) – New indication

- On January 15, 2021, Daiichi Sankyo and AstraZeneca announced the FDA approval of Enhertu (fam-trastuzumab deruxtecan-nxki), for the treatment of adult patients with locally advanced or metastatic human epidermal growth factor receptor 2 (HER2)-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumab-based regimen.

- Enhertu is also approved for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting.

- The approval of Enhertu for the new indication was based on DESTINY-Gastric01, an open-label, randomized study in 188 adult patients with HER2-positive, locally advanced or metastatic gastric or GEJ adenocarcinoma who had progressed on at least two prior regimens. Patients were randomized to Enhertu or physician's choice of chemotherapy: irinotecan monotherapy or paclitaxel monotherapy. The major efficacy outcomes were objective response rate (ORR) and overall survival (OS). Additional efficacy outcomes were progression-free survival (PFS) and duration of response (DOR).

    - The ORR was 40.5% vs. 11.3% with Enhertu vs. chemotherapy, respectively ($p < 0.0001$).
    - Median OS was 12.5 months vs. 8.4 months (hazard ratio [HR] 0.59, 95% CI: 0.39, 0.88; $p = 0.0097$).
    - Median PFS was 5.6 months vs. 3.5 months with Enhertu vs. chemotherapy, respectively (HR 0.47, 95% CI: 0.31, 0.71).
    - Median DOR was 11.3 months vs. 3.9 months with Enhertu vs. chemotherapy, respectively.

- Enhertu carries a boxed warning for interstitial lung disease and embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%) with Enhertu use for gastric cancer were decreased hemoglobin, decreased white blood cell count, decreased neutrophil count, decreased lymphocyte count, decreased platelet count, nausea, decreased appetite, anemia, increased aspartate aminotransferase, fatigue, increased blood alkaline phosphatase, increased alanine aminotransferase, diarrhea, hypokalemia, vomiting, constipation, increased blood bilirubin, pyrexia, and alopecia.

- The recommended dose of Enhertu for the treatment of gastric cancer is 6.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity.

    - Patients with locally advanced or metastatic gastric cancer should be selected based on HER2 protein overexpression or HER2 gene amplification. Reassess HER2 status if it is feasible to obtain a new tumor specimen after prior trastuzumab-based therapy and before treatment with Enhertu.
    - Information on FDA-approved tests for the detection of HER2 protein overexpression and HER2 gene amplification in gastric cancer is available at: http://www.fda.gov/CompanionDiagnostics.

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— Refer to the Enhertu drug label for dosing for breast cancer.

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