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

- On May 5, 2022, Daiichi Sankyo and AstraZeneca announced the FDA approval of Enhertu (fam-trastuzumab deruxtecan-nxki), for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received a prior anti-HER2-based regimen either:
    - In the metastatic setting, or
    - In the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy.
- Enhertu was previously granted accelerated approval for 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.
- Enhertu is also approved for the treatment of adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumab-based regimen.
- The approval of Enhertu for the expanded indication was based on DESTINY-Breast03, an open-label, randomized study in 524 patients with HER2-positive, unresectable and/or metastatic breast cancer who received prior trastuzumab and taxane therapy for metastatic disease or developed disease recurrence during or within 6 months of completing adjuvant therapy. Patients were randomized to receive either Enhertu or Kadcyla® (ado-trastuzumab emtansine) every 3 weeks until unacceptable toxicity or disease progression. The major efficacy outcomes were progression-free survival (PFS) and overall survival (OS). Confirmed objective response rate (ORR) was an additional outcome measure.
    - Median PFS was not reached with Enhertu vs. 6.8 months with Kadcyla (hazard ratio 0.28, 95% CI: 0.22, 0.37; $p < 0.0001$).
    - At the time of the PFS analysis, 16% of patients had died and OS was immature.
    - ORR was 82.7% (95% CI: 77.4, 87.2) and 36.1% (95% CI: 30.0, 42.5) with Enhertu and Kadcyla, respectively.
- Enhertu carries a boxed warning for interstitial lung disease and embryo-fetal toxicity.
- The recommended dosage of Enhertu for metastatic breast cancer is 5.4 mg/kg given as an intravenous (IV) infusion once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity.
    - Enhertu should not be substituted for or with trastuzumab or Kadcyla.
    - Refer to the Enhertu drug label for dosing for gastric cancer.