Enhertu® (fam-trastuzumab deruxtecan-nxki) – New drug approval

- On December 20, 2019, the FDA announced the approval of Daiichi Sankyo's Enhertu (fam-trastuzumab deruxtecan-nxki), for the treatment of adult patients with unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting.
    - This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- Approximately one of every five breast cancers have a gene mutation in the cancer cells that makes an excess of the HER2 protein. HER2-positive breast cancers are an aggressive type of breast cancer.
- Enhertu is a HER2-directed antibody and topoisomerase inhibitor conjugate.
- The efficacy of Enhertu was evaluated in a single-arm study (DESTINY-Breast01) that enrolled 184 female patients with HER2-positive, unresectable and/or metastatic breast cancer who had received two or more prior anti-HER2 therapies. Patients received Enhertu every 3 weeks until unacceptable toxicity or disease progression. The major efficacy outcomes were confirmed objective response rate (ORR) and duration of response (DOR).
    - The ORR was 60.3% (95% CI: 52.9, 67.4).
    - The DOR was 14.8 months (95% CI: 13.8, 16.9).
- Enhertu carries a boxed warning for interstitial lung disease and embryo-fetal toxicity.
- Additional warnings and precautions of Enhertu include interstitial lung disease/pneumonitis, neutropenia, and left ventricular dysfunction.
- The most common adverse reactions (≥ 20%) with Enhertu use were nausea, fatigue, vomiting, alopecia, constipation, decreased appetite, anemia, neutropenia, diarrhea, leukopenia, cough, and thrombocytopenia.
- The recommended dose of Enhertu is 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity.
    - Do not substitute Enhertu for or with trastuzumab or ado-trastuzumab emtansine (Kadcyla®).
- Daiichi Sankyo's launch plans for Enhertu are pending. Enhertu will be available as a 100 mg lyophilized powder in a single dose vial.