HEM/ONC News

By Stacey Small

FDA Panel Supports Accelerated Approval of Pertuzumab for Neoadjuvant Treatment in HER2-Positive, Early-Stage Breast Cancer

On September 12, the US Food and Drug Administration's (FDA) Oncologic Drugs Advisory Committee (ODAC) panel voted 13:0, with 1 abstention, in favor of recommending accelerated approval of a pertuzumab (Perjeta, Genentech) regimen for neoadjuvant treatment in patients with high-risk, human epidermal growth factor receptor 2 (HER2)-positive, early-stage breast cancer. If approved, pertuzumab would be the first neoadjuvant breast cancer treatment and the first treatment approved based on pathologic complete response data.

Pertuzumab was approved in 2012 as a first-line treatment for metastatic HER2-positive breast cancer in patients who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease. The FDA is reviewing pertuzumab in the neoadjuvant early breast cancer setting as a potential accelerated approval. If approved for this expanded use, pertuzumab would be specifically indicated for the neoadjuvant treatment of breast cancer, in combination with trastuzumab (Herceptin, Genentech) and docetaxel, for patients with HER2-positive, locally advanced, inflammatory, or early-stage breast cancer (>2 cm in diameter), as part of a complete early breast cancer regimen containing fluorouracil, epirubicin, and cyclophosphamide (FEC) or carboplatin.

The ODAC recommendation was based on a review of results from 2 phase 2 studies. In the NEOSPHERE (Neoadjuvant Study of Pertuzumab and Herceptin in an Early Regimen Evaluation) study, treatment with pertuzumab, trastuzumab, and docetaxel chemotherapy significantly improved the rate of total pathologic complete response by 17.8% when compared with trastuzumab and docetaxel alone (39.3% vs 21.5%, respectively; P=.0063). In the TRYPHAENA (Trastuzumab Plus Pertuzumab in Neoadjuvant HER2-Positive Breast Cancer) study, the combination of pertuzumab plus trastuzumab in the neoadjuvant setting achieved pathologic complete response rates ranging from approximately 55% to 64% in combination with various chemotherapy regimens. Longer-term safety data from the phase 3 CLEOPATRA (Clinical Evaluation of Pertuzumab and Trastuzumab) study of pertuzumab in HER2-positive metastatic breast cancer were also reviewed.

Should pertuzumab receive accelerated approval for its expanded use, its full approval will be contingent on the final results of the confirmatory APHINITY (Adjuvant Pertuzumab and Herceptin in Initial Therapy of Breast Cancer) study, which will compare chemotherapy plus trastuzumab with or without pertuzumab before surgery in approximately 4800 patients with HER2-positive early breast cancer. The patients will be followed for 10 years, and the study will evaluate invasive disease-free survival. The first available results are expected in 2016.

First Generic Version of Capecitabine Approved for Use in Metastatic Breast and Colorectal Cancer

On September 16, the FDA announced its approval of the first generic version of capecitabine (Xeloda, Genentech). Capecitabine is approved for the treatment of metastatic colorectal and breast cancer.

The drug is most well known for its use in combination strategies, specifically in HER2-positive metastatic breast cancer, where it is commonly administered along with lapatinib (Tykerb, GlaxoSmithKline). When administered as monotherapy, capecitabine has demonstrated efficacy in the first-line setting for patients with metastatic colorectal cancer following complete resection of the primary tumor when fluoropyrimidine therapy is preferred, and as a treatment for patients with HER2-negative metastatic breast cancer following prior treatment with anthracyclines and taxanes. More than 300 ongoing studies are examining the drug in combination or as a single-agent across a variety of diseases.

Teva Pharmaceuticals USA will market generic capecitabine in 150 and 500 mg strengths. According to the FDA, on average, the cost of a generic drug is 80% to 85% lower than the brand name equivalent.

Common adverse events observed in clinical trials involving capecitabine included diarrhea, vomiting, and nausea, as well as oral pain, redness, swelling, and sores. Other events were hand-foot syndrome, fever, and infection. Like its brand-name equivalent, the generic agent will carry a boxed warning about a drug-drug interaction that increases bleeding risk for patients who taking anticoagulants (eg, warfarin).