HEM/ONC News

By Devon Schuyler

FDA Approves Ceritinib in Metastatic ALK-Positive NSCLC

The US Food and Drug Administration has granted accelerated approval to ceritinib (Zykadia, Novartis) as a treatment for patients with metastatic anaplastic lymphoma kinase (ALK)–positive non–small cell lung cancer (NSCLC) who have received crizotinib (Xalkori, Pfizer).

The approval was based on results from a single-arm, open-label clinical trial of 163 patients with metastatic ALK-positive NSCLC who had progressed on crizotinib or were unable to tolerate it. Patients received one 750-mg dose of ceritinib per day in capsule form.

The overall response rate to ceritinib was 54.6% (95% CI, 47%-62%), and the median duration of response was 7.4 months (95% CI, 5.4-10.1 months). The most common adverse reactions were diarrhea, nausea, vomiting, abdominal pain, fatigue, decreased appetite, and constipation, each of which affected more than 25% of patients.

Ceritinib works by selectively inhibiting ALK. The *ALK* gene promotes the development and growth of cancer cells by fusing with other genes. Approximately 2% to 7% of patients with NSCLC test positive for the *ALK* gene.

The agent continues to be studied in several phase 2 and 3 trials of treatment-naive and previously treated patients. Ceritinib has not been shown to improve survival or disease-related symptoms.

ASCO Issues Guidelines on Treating Patients With Advanced, HER2-Positive Breast Cancer

The American Society of Clinical Oncology (ASCO) has issued 2 clinical practice guidelines for treating women with advanced, human epidermal growth factor receptor 2 (HER2)–positive breast cancer. Both guidelines were published ahead of print in the *Journal of Clinical Oncology* on May 5.

The first guideline, which addressed systemic treatment, was based on a systematic review of the literature on HER2-targeted therapies. A total of 16 randomized phase 3 clinical trials met the inclusion criteria. Based on the review, the panelists recommended that first-line therapy consist of a combination of trastuzumab (Herceptin, Genentech), pertuzumab (Perjeta, Genentech), and a taxane, and that second-line therapy consist of trastuzumab emtansine (TDM-1; Kadcyla, Genentech). They stated that third-line therapy and beyond depended on what agents patients had already received, but options included trastuzumab emtansine or pertuzumab if not already used, capecitabine with lapatinib (Tykerb, GlaxoSmithKline), trastuzumab alone or with lapatinib, and hormonal therapy.

The second guideline, which addressed brain metastases, was based on consensus because relevant research was relatively limited. The panelists recommended that surgery and/or radiotherapy be used in eligible patients with a favorable prognosis for survival, and that surgery, whole brain radiation therapy, and systemic therapies be considered for patients with a poor prognosis for survival.

Overexpression of the HER2 protein occurs in approximately 15% to 20% of patients with breast cancer. As many as half of patients with HER2-positive metastatic breast cancer develop brain metastases.

Obesity Linked to Breast Cancer Mortality Only in Premenopausal ER-Positive Disease

Obesity is associated with an increase in breast cancer mortality among premenopausal women with estrogen receptor (ER)–positive disease, according to a study being presented at the ASCO annual meeting. The study found that obesity had little relationship to breast cancer mortality in women with postmenopausal ER-positive disease or in those with ER-negative disease.

This finding was based on an analysis from the Early Breast Cancer Trialists' Collaborative Group of 80,000 patients in 70 trials, who were followed for an average of 8 woman-years. The researchers, led by Dr Hongchao Pan, found only a weak link between higher body mass index (BMI) and breast cancer mortality among 20,000 women with ER-negative disease; the association disappeared after adjusting for tumor diameter and nodal status.

Among the 60,000 women with ER-positive disease, BMI was associated with breast cancer mortality in premenopausal and postmenopausal women. After adjusting for tumor characteristics, the association remained statistically significant only in the 20,000 premenopausal women with ER-positive disease; breast cancer mortality was 34% higher in obese women (BMI, 30 or higher) than in normal-weight women (BMI, 20-24.9).

The authors were surprised that obesity adversely affected outcomes only in premenopausal women because obesity substantially increases circulating estrogen levels only in postmenopausal women.