HEM/ONC News

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FDA Approves Palbociclib for Breast Cancer

Palbociclib (Ibrance, Pfizer) has received accelerated approval from the US Food and Drug Administration (FDA) for use in combination with letrozole (Femara, Novartis) for advanced breast cancer.

The drug is indicated for postmenopausal women with estrogen receptor (ER)–positive, human epidermal growth factor receptor 2 (HER2)–negative metastatic breast cancer who have not received an endocrine-based therapy. Palbociclib is an inhibitor of cyclin-dependent kinases 4 and 6, which play a role in the growth of cancer cells.

The February approval was based on results from the phase 2 PALOMA-1 study, which included 165 postmenopausal women with ER-positive, HER2-negative advanced breast cancer who had not been treated for advanced disease. Participants were randomly assigned to receive either letrozole plus palbociclib or letrozole alone. After a median follow-up of 27.9 to 29.6 months, progression-free survival was significantly higher in patients who received letrozole plus palbociclib (20.2 months) than in those who received letrozole alone (10.2 months). There was no evidence of improvement in overall survival. The study was published in the January 2015 issue of *Lancet Oncology.*

The most common side effects of palbociclib were neutropenia, leukopenia, fatigue, anemia, upper respiratory infection, nausea, stomatitis, alopecia, diarrhea, thrombocytopenia, decreased appetite, vomiting, asthenia, peripheral neuropathy, and epistaxis.

A phase 3 study of palbociclib called PALOMA-2 is underway (NCT01740427).

Ibrutinib Receives Indication for Waldenström Macroglobulinemia

Ibrutinib (Imbruvica, Pharmacyclics/Janssen Biotech) has received a new indication, for the treatment of Waldenström macroglobulinemia (WM). Ibrutinib is a Bruton's kinase inhibitor that works by blocking the enzyme that allows the abnormal B-cells in WM to grow and divide.

The FDA first approved ibrutinib in November 2013 for use in patients with mantle cell lymphoma who had received 1 prior therapy. The agent received a second indication, for patients with previously treated chronic lymphocytic leukemia, in February 2014. In July 2014, the agent received an additional approval for use in patients with chronic lymphocytic leukemia who carry a deletion in chromosome 17.

The approval of ibrutinib was based on a study of 63 people with WM who had previously been treated. All of the patients in the study received a daily 420-mg dose of the medication by mouth until the disease progressed or side effects became intolerable. The overall response rate was 62%, and the duration of response ranged from 2.8 months to 18.8 months.

The most common side effects associated with ibrutinib are thrombocytopenia, neutropenia, diarrhea, anemia, fatigue, musculoskeletal pain, bruising, nausea, upper respiratory tract infection, and rash. There is also a risk of hemorrhage, infections, atrial fibrillation, second primary malignancies, tumor lysis syndrome, and embryo-fetal toxicity.

Ibrutinib for use in WM received breakthrough therapy designation, priority review, and orphan product designation.

FDA Approves Lenvatinib for Progressive, Differentiated Thyroid Cancer

Lenvatinib (Lenvima, Eisai) has been approved by the FDA for patients with progressive, differentiated, radioiodine-refractory thyroid cancer. Lenvatinib inhibits multiple kinases that help the cancer cells grow and divide.

The approval was based on results from the phase 3 SELECT (Study of [E7080] Lenvatinib in Differentiated Cancer of the Thyroid) trial, published in the *New England Journal of Medicine* in February 2015.

For this trial, researchers randomly assigned patients to either 24 mg per day of oral lenvatinib in 28-day cycles (261 patients) or placebo (131 patients). After a median follow-up of 17.1 to 17.4 months, median progression-free survival was significantly longer in the lenvatinib group (18.3 months) than in the placebo group (3.6 months). An improvement in progression-free survival with lenvatinib was found in all the subgroups tested, including patients who had previously received treatment with a tyrosine kinase inhibitor. The response rate was significantly higher in patients receiving lenvatinib than in those receiving placebo (64.8% vs 1.5%, respectively). Median overall survival could not be estimated in either group.

The most common side effects of lenvatinib were hypertension, diarrhea, fatigue, decreased appetite, decreased weight, and nausea. Other serious side effects included cardiac failure, arterial thromboembolic events, hepatotoxicity, and renal failure. Six of 20 deaths in the lenvatinib group were considered treatment-related, including 1 pulmonary embolism and 1 hemorrhagic stroke.