HEM/ONC News

By Devon Schuyler

FDA Approves Ibrutinib for Use in Chronic Lymphocytic Leukemia

The US Food and Drug Administration (FDA) approved ibrutinib (Imbruvica, Pharmacyclics/Janssen Biotech) on February 12 for use in patients with chronic lymphocytic leukemia (CLL) who have received at least 1 prior therapy. Ibrutinib was previously approved in November 2013 for patients with mantle cell lymphoma who have received at least 1 prior therapy.

The approval, which was granted through the FDA's accelerated approval program, was based on the results of a phase 1b/2, single-arm trial of 48 patients with relapsed or refractory CLL. All patients received 420 mg per day of ibrutinib orally until disease progression or unacceptable toxicity. The overall response rate was 58.3% (95% CI, 43.2%-72.4%), and all responses were partial responses. The duration of response ranged from 5.6 to 24.2-plus months; the median duration of response was not reached.

The most common adverse reactions were thrombocytopenia, diarrhea, bruising, neutropenia, anemia, upper respiratory tract infection, fatigue, musculoskeletal pain, rash, pyrexia, constipation, peripheral edema, arthralgia, nausea, stomatitis, sinusitis, and dizziness. A total of 5 patients discontinued the drug because of side effects that included infections and subdural hematomas.

Both of ibrutinib's indications are based on overall response rate. Improvement in survival or disease-related symptoms has not been established.

Adjuvant Chemotherapy Does Not Improve Survival in Rectal Cancer

Adjuvant chemotherapy has no effect on survival from rectal cancer, according to a new study in the February issue of *Lancet Oncology* that followed patients for a median of more than 10 years. The study confirmed earlier results from this and other trials showing that chemotherapy (both neoadjuvant and adjuvant) does improve local control.

For the European Organisation for Research and Treatment of Cancer (EORTC) 22921 study, led by Jean-François Bosset, researchers randomly assigned 1011 patients with stage T3 or T4 resectable rectal cancer to one of 4 groups: preoperative radiotherapy, preoperative chemoradiotherapy, preoperative radiotherapy plus postoperative chemotherapy, and preoperative chemoradiotherapy plus postoperative chemotherapy. Chemotherapy consisted of fluorouracil and leucovorin.

The use of adjuvant chemotherapy did not affect overall survival at 10 years. The overall survival rate was 51.8% for those who received adjuvant chemotherapy vs 48.4% for those who did not (HR, 0.91; 95% CI, 0.77-1.09; *P*=.32). Adjuvant chemotherapy also had no effect on disease-free survival, the cumulative incidence of distant metastases, or the frequency of long-term side effects.

By contrast, the cumulative incidence of local relapse at 10 years was 22.4% with preoperative radiotherapy alone, 11.8% with neoadjuvant radiotherapy plus chemotherapy, 14.5% with radiotherapy plus adjuvant chemotherapy, and 11.7% with both neoadjuvant and adjuvant chemotherapy (*P*=.0017).

According to a commentary by Geerard Beets and Bengt Glimelius that accompanied the study, "the most important information provided by the trial is that chemotherapy is poorly tolerated after surgery for rectal cancer," as more than half the patients did not receive the planned 4 cycles. They suggested that until more is known, neoadjuvant chemotherapy—which is being studied in several trials of rectal cancer—may be a logical approach to treatment.

Lenvatinib Improves Progression-Free Survival in Thyroid Cancer

The investigational tyrosine kinase inhibitor lenvatinib has been shown in a phase 3 trial to improve progression-free survival in patients with differentiated thyroid cancer that is refractory to radioiodine, according to Eisai, the drug's manufacturer.

The trial, called SELECT (Study of E7080 Lenvatinib in Differentiated Cancer of the Thyroid), included 392 patients with radioiodine-refractory differentiated thyroid cancer and radiographic evidence of disease progression within the previous 12 months. Patients were randomly assigned to receive either lenvatinib 24 mg once daily or a placebo.

SELECT met its primary endpoint when the investigators found that lenvatinib significantly improved progression-free survival; secondary endpoints included overall response rate, overall survival, and safety. The most common adverse effects were hypertension, diarrhea, decreased appetite, weight loss, and nausea.

Lenvatinib is an investigational small molecule tyrosine kinase inhibitor that inhibits vascular endothelial growth factor receptors 1 to 3, fibroblast growth factor receptors 1 to 4, platelet-derived growth factor receptor-β, Kit, and proto-oncogene tyrosine-protein kinase receptor Ret, all of which are involved in angiogenesis and tumor proliferation. Eisai is planning to submit marketing applications for lenvatinib in the United States, Europe, and Japan.