PHARMACY CORNER

New Treatment Available for Non-Small Cell Lung Cancer

Crizotinib (Xalkori®), an oral anaplastic lymphoma kinase (ALK) inhibitor, has received U.S. Food and Drug Administration (FDA) approval for the treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) that has tested positive for ALK gene abnormalities.

In two single-arm clinical trials (studies A and B), patients with ALK-positivity demonstrated significant objective response (OR) rates to treatment with crizoitnib. In study A (N = 136), 50% of patients demonstrated OR with a median duration of response (MDR) of 41.9 weeks. In study B (N = 119), 61% of patients demonstrated OR with a MDR of 48.1 weeks. In the two studies, only three patients (1%) experienced complete responses.

Of the 255 patients enrolled, the majority (n = 241) had metastatic disease, and the primary histology of patients was adenocarcinoma (n = 246). Of interest, 178 (70%) of the patients enrolled had never smoked. Only six patients (2%) were current smokers on study enrollment. A nonsmoking history appears to increase the chances of ALK-positive findings, and in patients for whom epidermal growth factor inhibitors (e.g., erlotinib) are not a viable or effective treatment, crizotinib may provide another promising option.

FDA approval was granted based on OR rates, as clinical data demonstrating impact on survival are not yet available. Pfizer is recruiting patients for a phase III clinical trial to determine if crizotinib prolongs progression-free survival compared to standard chemotherapy with pemetrexed (Alimta®) or docetaxel (Taxotere®) in patients with ALK-positive NSCLC.

ALK-positive tumors can be detected through use of the Vysis ALK Break-Apart FISH Probe Kit. For patients who test positive for ALK gene abnormality, crizotinib demonstrates the continuing importance of developing targeted therapies for cancer. Use of crizotinib as first-line therapy now is included in the National Comprehensive Cancer Network guidelines for patients with ALK-positive histology.

Unfortunately, only a small percentage of NSCLC tumors can be expected to respond to crizotinib therapy, as the incidence of ALK-positivity occurs in only 4%–5% of all NSCLC tumors. However, with the prevalence of lung cancer, even that small percentage represents a large number of patients, with an estimated 40,000 ALK-positive NSCLC cases annually worldwide.

The drug typically is dosed as 250 mg capsules by mouth twice daily. Capsules should not be crushed, dissolved, or opened. Crizotinib may be taken without regard to meal time, but patients should not drink grapefruit juice while on therapy. As crizotinib is metabolized via the CYP3A pathway, intake of grapefruit juice (a strong CYP3A inhibitor) could lead to toxic serum levels of crizotinib.

Common treatment-related adverse events include vision changes (62%), nausea (53%), diarrhea (43%), vomiting (40%), edema (28%), and constipation (27%). Although uncommon, serious reactions such as pneumonitis (2%) may occur and necessitate treatment discontinuation. Patients should be monitored for hepatic and cardiac toxicities; if observed, treatment breaks until resolution of toxicities, with subsequent dose reduction according to manufacturer guidelines, should occur. In severe cases (e.g., grade 4 QTc prolongation, elevated liver enzymes with a rise in total bilirubin), treatment discontinuation may be required.

For more information, visit www.accessdata.fda.gov/drugsatfda_docs/label/2011/202570s000lbl.pdf.

Monoclonal Antibody Receives Approval for Lymphomas

A new chimeric CD30-directed monoclonal antibody, brentuximab vedotin (Adcetris™), has received FDA approval for the treatment of Hodgkin lymphoma after autologous hematopoietic progenitor stem cell transplantation (AHPSCT) failure, as well as for the treatment of patients who do not qualify for AHPSCT. In addition, the drug has received approval to treat systemic anaplastic large cell lymphoma (ALCL) refractory to chemotherapy. This is biotechnology company Seattle Genetics' first FDA-approved drug. Approval was granted based on response rates, and data on patient outcomes and survival are not yet available.

In a single-arm clinical trial using brentuximab to treat Hodgkin lymphoma following failure of AHPSCT (N = 102), 73% of patients achieved OR, with 32% achieving complete remission. The median duration of OR was 6.7 months.

In a single-arm clinical trial using brentuximab to treat relapsed ALCL (N = 58), 86% of patients obtained OR, with 57% achieving complete remission. The median duration of OR was 12.6 months.

For both indications, the drug typically is dosed at 1.8 mg/kg and given via IV over 30 minutes every three weeks for a maximum of 16 cycles. As with other monoclonal antibodies, the risk for infusion reactions exists, and nurses should monitor for and treat appropriately. Package insert directions do not suggest the need for premedication to prevent initial infusion reactions, but in patients who have experienced infusion reactions, consideration should be given to premedicating subsequent doses with agents such as acetaminophen, antihistamines, and corticosteroids.

Adverse reactions include sensory peripheral neuropathy and neutropenia. Based on severity, treatment breaks or dosage reductions may be required. In clinical trials, 54% of patients experienced some degree of neuropathy and, of these, 49% had complete resolution of neuropathy following treatment cessation. About 21% of patients experienced grade 3 or 4 neutropenia, so patients should be instructed regarding reporting signs of infection (e.g., fever) and measures to prevent infection. Growth factor support should be considered in patients who experience or are anticipated to experience grade 3 or 4 neutropenia. Other cytopenias (e.g., anemia, thrombocytopenia) were less common.

For more information, visit www.accessdata.fda.gov/drugsatfda_docs/label/2011/125388s000,125399s000lbl.pdf.

Melanoma Drug Approved for Patients With *BRAFV600E*

Vemurafenib (Zelboraf®) received FDA approval for the treatment of unresectable or metastatic melanoma exhibiting the *BRAFV600E* mutation, which is present in more than half of cutaneous melanomas. As previously