HEM/ONC News

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Osimertinib Approved for Use in NSCLC

The US Food and Drug Administration (FDA) approved osimertinib (Tagrisso, AstraZeneca) on November 13 for use in patients with advanced non–small cell lung cancer (NSCLC) who have the epidermal growth factor receptor (*EGFR*) T790 mutation and disease progression after treatment with another EGFR inhibitor.

The FDA also approved a companion diagnostic test, the cobase EGFR Mutation Test v2 from Roche, to detect the *EGFR* T790 mutation.

Approval of osimertinib was based on the results of 2 single-arm studies that enrolled a total of 411 patients with advanced NSCLC that was positive for the *EGFR* T790 mutation and that had worsened after treatment with an EGFR inhibitor. The objective response rate to osimertinib was 57% in the first study and 61% in the second study.

Potential side effects of osimertinib include diarrhea, dry skin, rash, and infection or redness around the fingernails. Serious side effects include inflammation of the lungs and injury to the heart.

FDA Approves Cobimetinib for Advanced Melanoma

The FDA approved cobimetinib (Cotellic, Roche) on November 10 for use in combination with vemurafenib (Zelboraf, Genentech/Daiichi Sankyo) as a treatment for unresectable advanced melanoma that is positive for the *BRAF* V600 mutation. Cobimetinib is a MEK inhibitor.

Approval of the combination was based on a study of 495 patients with previously untreated, unresectable, locally advanced or metastatic melanoma that was *BRAF* V600 mutation–positive. Patients were randomly assigned to receive vemurafenib plus either cobimetinib or placebo.

The median progression-free survival was significantly higher with combination treatment than with vemurafenib alone: 12.3 months vs 7.2 months. The rate of complete or partial response also was higher in the combination group than in the control group: 70% vs 50%. The 17-month survival rate was higher with combination treatment than with vemurafenib alone: 65% vs 50%.

The most common side effects of vemurafenib/cobimetinib were diarrhea, photosensitivity, nausea, pyrexia, and vomiting. Cobimetinib also may cause cardiomyopathy, rhabdomyolysis, primary cutaneous malignancies, retinal detachment, severe skin rash, hepatotoxicity, and hemorrhage.

FDA Approves Trabectedin for Soft Tissue Sarcoma

The FDA approved trabectedin (Yondelis, Janssen) on October 23 for treatment of patients with unresectable or metastatic liposarcoma or leiomyosarcoma. The agent is for use in patients who previously received anthracycline-containing chemotherapy.

Approval of trabectedin was based on a trial of 518 patients with metastatic or recurrent liposarcoma or leiomyosarcoma. Patients were randomly assigned to receive either trabectedin (345 patients) or dacarbazine (173 patients). Mean progression-free survival was 4.2 months with trabectedin vs 1.5 months with dacarbazine.

The most common side effects with trabectedin were nausea, fatigue, vomiting, diarrhea, constipation, decreased appetite, dyspnea, headache, peripheral edema, neutropenia, thrombocytopenia, anemia, elevated liver enzymes, and decreases in albumin.

Serious side effects include neutropenic sepsis, rhabdomyolysis, hepatotoxicity, extravasation, tissue necrosis, and cardiomyopathy.

Idarucizumab Approved for Anticoagulation Reversal

The FDA approved idarucizumab (Praxbind, Boehringer Ingelheim) on October 16 for the reversal of anticoagulation in patients treated with dabigatran (Pradaxa, Boehringer Ingelheim). Idarucizumab is indicated for use when emergency or urgent surgery is required, or when bleeding is uncontrolled or life-threatening.

Approval of idarucizumab was based on 3 trials that enrolled a total of 283 healthy volunteers. The participants were randomly assigned to dabigatran plus either idarucizumab or placebo. The researchers found that 5 g of idarucizumab reduced the amount of unbound dabigatran to undetectable levels in the plasma.

An ongoing open-label trial is looking at the use of idarucizumab in patients on dabigatran who require emergency or urgent surgery, or who have uncontrolled or life-threatening bleeding. Of the 123 patients who have been studied so far, the anticoagulant effect of dabigatran was completely reversed in more than 89% of patients within 4 hours of idarucizumab administration.

The most common side effects of idarucizumab, according to data from the 123 patients and from 224 healthy volunteers, were headache, hypokalemia, delirium, constipation, pyrexia, and pneumonia.