HEM/ONC News

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New Formulation of Melphalan Approved for Multiple Myeloma

The US Food and Drug Administration (FDA) approved Captisol-enabled melphalan (Evomela, Spectrum) on March 16 for 2 indications in patients with multiple myeloma: as a high-dose conditioning treatment before hematopoietic stem cell transplant (HSCT) and as a palliative treatment when oral therapy is not appropriate.

Captisol is a modified form of cyclodextrin that improves the solubility and stability of melphalan, eliminating the need for propylene glycol. Propylene glycol has been linked to metabolic/renal dysfunction and arrhythmias.

Approval was based on the results of a phase 2b, open-label study conducted by Hari and colleagues and published in 2015 in the journal *Biology of Blood and Marrow Transplantation.* The study included 61 patients with multiple myeloma: 5 who had experienced relapse before HSCT and 56 who had a new diagnosis.

All patients achieved myoablation, which occurred at a median of 5 days after surgery; neutrophil engraftment, which occurred a median of 12 days after surgery; and platelet engraftment, which occurred a median of 13 days after surgery. An independent, blinded review on day 100 after surgery revealed an overall response rate of 100% and a complete response rate of 21%. No treatment-related mortality occurred, and most nonhematologic adverse events were grade 1 or 2.

Captisol-enabled melphalan is the first drug to receive FDA approval for use as a high-dose conditioning agent in multiple myeloma.

FDA Expands Crizotinib Approval to *ROS1*-Mutated Lung Cancer

The FDA expanded the indications for crizotinib (Xalkori, Pfizer) on March 11 to *ROS1*-mutated metastatic non–small cell lung cancer (NSCLC). Crizotinib is the first treatment to receive approval for patients with *ROS1*-positive NSCLC. Approximately 1% of patients with NSCLC have alterations in the *ROS1* gene.

The expanded indication was based on the results of a single-group study of 50 patients with metastatic NSCLC that harbored the mutated form of *ROS1*. The tumors responded to treatment in 66% of patients.

The most common adverse events associated with crizotinib are vision disorders, nausea, diarrhea, vomiting, edema, constipation, elevated transaminases, fatigue, decreased appetite, upper respiratory infection, dizziness, and neuropathy. Serious side effects include liver problems, severe lung inflammation, irregular heartbeat, and vision loss.

Crizotinib was previously approved for use in patients with locally advanced or metastatic *ALK*-positive NSCLC.

Coagulation Factor-Albumin Fusion Protein Approved for Hemophilia B

The FDA approved recombinant coagulation factor IX, albumin fusion protein (Idelvion, CSL Behring) on March 4 for use in adults and children with hemophilia B. This is the first coagulation factor–albumin fusion protein product to receive approval. It is used to prevent and treat episodes of bleeding, including bleeding after surgery.

Approval was based on 2 multicenter studies that included a total of 90 children and adults between the ages of 1 and 61 years with hemophilia B. The agent was shown to be effective for the control of episodes of bleeding and the management of perioperative bleeding. Prophylactic use of the agent significantly reduced the rate of episodes of spontaneous bleeding.

The most common side effect was headache, and the studies did not identify any safety concerns.

FDA Approves Recombinant Factor VIII Concentrate for Hemophilia A

On March 17, the FDA approved a recombinant antihemophilic factor (Kovaltry, Bayer) for use in adults and children with hemophilia A. The product is a recombinant, full-length factor VIII concentrate derived from human DNA that supports hemostasis by temporarily replacing factor VIII. It is indicated for the treatment and control of episodes of bleeding, the perioperative management of bleeding, and routine prophylaxis to reduce episodes of bleeding.

Approval was based on the LEOPOLD trials, a series of open-label, crossover, uncontrolled studies in patients younger than 65 years. The studies found that the efficacy of on-demand treatment for episodes of bleeding was "good" or "excellent" in 90% of cases, that hemostatic control during surgery was "good" or "excellent," and that prophylactic treatment vs on-demand treatment reduced the number of episodes of bleeding from 60 to 2 per year.

Side effects include headache, pyrexia, and pruritus.