HEM/ONC News

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FDA Approves First US Biosimilar

The US Food and Drug Administration (FDA) recently approved filgrastim-sndz (Zarxio, Sandoz) as a biosimilar to filgrastim (Neupogen, Amgen), a granulocyte colony-stimulating factor for patients with a high risk of neutropenia. Although filgrastim-sndz was previously approved outside of the United States as Zarzio, it is the first biosimilar to be approved in the United States.

Approval was primarily based on PIONEER, a phase 3 randomized trial. Comparing the biosimilar with filgrastim, the researchers found no differences in the duration of severe neutropenia (1.17 vs 1.20 days, respectively) or in the mean time to absolute neutrophil count recovery during cycle 1 (1.8 days vs 1.7 days, respectively). Other studies also found the 2 drugs to be similar by structural and functional characterization, animal study data, human pharmacodynamics data, clinical immunogenicity data, and other clinical safety and effectiveness data.

All of these data were important for approval, because the FDA requires biosimilars to have the same mechanism(s) of action, route(s) of administration, dosage forms(s), and strength(s) as the original product. Biosimilars also must not have any clinically meaningful differences in safety or efficacy.

Filgrastim-sndz was approved for the same indications as filgrastim, including patients with cancer receiving myelosuppressive chemotherapy. This approval paves the way for other biosimilars, which are expected to improve availability and reduce the cost of these drugs.

Carfilzomib Found Superior to Bortezomib in Patients With Relapsed Multiple Myeloma

Carfilzomib is superior to bortezomib (Velcade, Millennium Pharmaceuticals) in patients with relapsed multiple myeloma, according to the results of a phase 3 study.

The ENDEAVOR study included 929 patients with multiple myeloma that had relapsed after 1 to 3 previous therapies. These patients were randomly assigned to receive low-dose dexamethasone with carfilzomib (Kyprolis, Onyx Pharmaceuticals) or with bortezomib.

Patients in the carfilzomib arm had significantly improved progression-free survival compared with the bortezomib arm (18.7 months vs 9.4 months, respectively). Patients treated with carfilzomib also had a better overall response rate and lower incidence of neuropathic events. Overall survival was not evaluated.

Treatment discontinuation was similar between the 2 groups; however, the rates of cardiac failure, renal failure, dyspnea, and hypertension were increased with carfilzomib vs bortezomib. Warnings for carfilzomib include cardiac arrest, heart failure, myocardial ischemia, pulmonary hypertension, pulmonary complications, infusion reactions, tumor lysis syndrome, thrombocytopenia, hepatic toxicity, and embryo-fetal toxicity. The most common serious adverse events were pneumonia, acute renal failure, pyrexia, and heart failure.

Carfilzomib, a selective proteasome inhibitor, was given accelerated approval by the FDA in July 2012 for patients with relapsed multiple myeloma.

FDA Expands Indication for Lenalidomide to Include Front-Line Multiple Myeloma

The FDA has expanded the use of lenalidomide (Revlimid, Celgene) with dexamethasone in multiple myeloma to include newly diagnosed patients. This combination was approved in June 2006 for patients with multiple myeloma who had received at least one previous therapy.

The new approval of this combination was based on results from multiple phase 3 studies, including the FIRST trial. Some of these results were published by Benboubker and colleagues in the *New England Journal of Medicine* in September 2014. The primary analysis of this trial compared the group receiving lenalidomide and dexamethasone in 28-day cycles until disease progression (535 patients) with the group receiving the standard therapy of melphalan, prednisone, and thalidomide for 72 weeks (547 patients). Secondary analysis included a third group of patients receiving lenalidomide and dexamethasone for 72 weeks (541 patients). All 1623 patients in the trial were newly diagnosed and not eligible for stem cell transplantation.

The primary analysis found that the group receiving continuous lenalidomide and dexamethasone had a significantly longer progression-free survival than the group receiving standard therapy (25.5 months vs 21.2 months, respectively). The patients receiving lenalidomide and dexamethasone also had a 25% reduction in the risk of death. The median overall survival was 58.9 months and 48.5 months, respectively.

The most common serious adverse events were neutropenia, anemia, thrombocytopenia, pneumonia, asthenia, fatigue, back pain, hypokalemia, rash, cataract, dyspnea, deep vein thrombosis, and hyperglycemia.