HEM/ONC News

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First Biosimilar to Pegfilgrastim Approved to Decrease Risk for Infection During Cancer Treatment

On June 4, the US Food and Drug Administration (FDA) approved pegfilgrastim-jmdb (Fulphila, Mylan), the first biosimilar to pegfilgrastim (Neulasta, Amgen), to decrease the risk for infection in patients with nonmyeloid cancer who have clinically significant febrile neutropenia while undergoing chemotherapy. Pegfilgrastim is a pegylated form of the recombinant human granulocyte colony–stimulating factor analogue filgrastim.

The most common side effects of pegfilgrastim-jmdb are bone pain and pain in the extremities. Patients with a history of serious allergic reactions to human granulocyte colony–stimulating factors should not receive the agent. Serious side effects of treatment with pegfilgrastim-jmdb include splenic rupture, acute respiratory distress syndrome, serious allergic reactions (including anaphylaxis), glomerulonephritis, leukocytosis, capillary leak syndrome, and the potential for tumor growth. Fatal sickle cell crises have occurred.

FDA Approves Venetoclax as Second-Line or Later Treatment of CLL or SLL

The FDA granted regular approval to venetoclax (Venclexta, AbbVie/Genentech) on June 8 for patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) who have received at least one prior therapy. The approval extends to patients with or without the 17p deletion.

Approval was based on MURANO (NCT02005471), a multicenter, open-label trial of 389 patients with CLL who had received at least one prior line of therapy. Patients were randomly assigned in a 1:1 ratio to venetoclax/rituximab (Rituxan, Genentech/Biogen) or bendamustine (Treanda/Bendeka, Teva)/rituximab.

After a median follow-up of 23 months, the median progression-free survival was not reached in the venetoclax arm vs 18.1 months (95% CI, 15.8%-22.3%) in the bendamustine arm (hazard ratio [HR], 0.19; 95% CI, 0.13-0.28; $P<.0001$). The overall response rate was 92% in the venetoclax arm vs 72% in the bendamustine arm.

The most common adverse reactions in the venetoclax group, with an incidence of at least 20%, were neutropenia, diarrhea, upper respiratory tract infection, fatigue, cough, and nausea. Grade 3 or 4 neutropenia developed in 64% of these patients, and grade 4 neutropenia in 31%. Serious adverse reactions occurred in 46% of patients. Serious infections developed in 21% of patients. Tumor lysis syndrome is an important identified risk with venetoclax treatment.

Pembrolizumab Approved for Advanced Cervical Cancer With Disease Progression During or After Chemotherapy

Pembrolizumab (Keytruda, Merck) received accelerated FDA approval on June 12 for patients with recurrent or metastatic cervical cancer whose disease has progressed on or after chemotherapy and whose tumors express programmed death ligand 1 (PD-L1).

This expanded indication for pembrolizumab was based on the multicenter, nonrandomized, open-label, multicohort KEYNOTE-158 trial (NCT02628067), in which 98 patients with recurrent or metastatic cervical cancer enrolled. Patients received pembrolizumab at a dose of 200 mg every 3 weeks until unacceptable toxicity or documented disease progression. Approval was based on results in the 77 patients whose tumors expressed PD-L1 with a combined positive score of at least 1 and who had received at least one line of chemotherapy for metastatic disease.

After a median follow-up of 11.7 months, the objective response rate was 14.3% (95% CI, 7.4%-24.1%). The estimated median duration of response, based on 11 patients with a response by independent review, was not reached. No responses were observed in patients whose tumors did not express PD-L1.

The most common adverse reactions, occurring in at least 10% of patients with cervical cancer enrolled in this trial, were fatigue, pain, pyrexia, peripheral edema, musculoskeletal pain, diarrhea/colitis, abdominal pain, nausea, vomiting, constipation, decreased appetite, hemorrhage, urinary tract infection, infections, rash, hypothyroidism, headache, and dyspnea. Adverse reactions leading to drug discontinuation occurred in 8% of patients. Serious adverse reactions occurred in 39% of patients.

Additional Approvals

- On June 7, the FDA approved methoxy polyethylene glycol-epoetin beta (Mircera, Vifor Pharma) for anemia associated with chronic kidney disease in patients aged 5 to 17 years who are on dialysis.
- On June 13, the FDA approved bevacizumab (Avastin, Genentech) in combination with chemotherapy, followed by single-agent bevacizumab, for patients with stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer after initial surgical resection.
- On June 13, the FDA also granted accelerated approval to pembrolizumab for the treatment of adult and pediatric patients with relapsed (after ≥2 prior lines of therapy) or refractory primary mediastinal large B-cell lymphoma.