HEM/ONC News

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First Gene Therapy Approved for Use in Acute Lymphoblastic Leukemia

The US Food and Drug Administration (FDA) has approved tisagenlecleucel (Kymriah, Novartis), the first chimeric antigen receptor T-cell therapy to receive approval, for use in acute lymphoblastic leukemia (ALL). The treatment received approval on August 30 for patients 25 years of age or younger who have B-cell precursor ALL that is refractory to treatment or is in second or later relapse.

Each dose of tisagenlecleucel is custom-made from the patient's own T cells, which are genetically modified to target leukemia cells that have the CD19 antigen on their surface.

Approval was based on the results of a single-arm clinical trial of 63 pediatric and young adult patients with relapsed or refractory B-cell precursor ALL. The overall remission rate after a single treatment was 83%, and 63% of patients had a complete remission.

Treatment with tisagenlecleucel has the potential to cause cytokine release syndrome; hospitals that provide this therapy must be specially certified and are required to have tocilizumab (Actemra, Genentech) available to treat this life-threatening side effect. Life-threatening neurologic events are also possible. Other severe side effects include serious infections, hypotension, acute kidney injury, fever, and hypoxia.

Novartis has set the price of tisagenlecleucel at $475,000.

FDA Reapproves Gemtuzumab for Acute Myeloid Leukemia

The FDA reapproved gemtuzumab ozogamicin (Mylotarg, Pfizer) on September 1 for 2 groups of patients with of CD33-positive acute myeloid leukemia (AML): adults with newly diagnosed disease and patients 2 years of age or older with relapsed or refractory disease. This antibody-drug conjugate targets the CD33 antibody.

Gemtuzumab ozogamicin was originally approved in May 2000 for older patients with CD33-positive AML who had experienced a relapse, but Pfizer voluntarily withdrew the drug from the market after subsequent trials prompted safety concerns and failed to confirm clinical benefit. The new approval is for a reduced dose and schedule in a different patient population.

Approval of gemtuzumab ozogamicin in combination with chemotherapy was based on a trial of 271 patients with newly diagnosed CD33-positive AML who were randomly assigned to receive daunorubicin/cytarabine either with or without gemtuzumab ozogamicin. Median event-free survival was significantly longer in the patients who received gemtuzumab ozogamicin than in those who did not (17.3 vs 9.5 months). The safety and efficacy of gemtuzumab ozogamicin as stand-alone treatment were established in 2 additional trials.

Common side effects include pyrexia, nausea, infection, vomiting, bleeding, thrombocytopenia, stomatitis, constipation, rash, headache, elevated liver function tests, and neutropenia. Severe side effects include low blood cell counts, infections, liver damage, hepatic veno-occlusive disease, infusion-related reactions, and hemorrhage.

Inotuzumab Ozogamicin Approved for B-Cell Acute Lymphoblastic Leukemia

On August 17, the FDA approved inotuzumab ozogamicin (Besponsa, Pfizer) for use in adults with relapsed or refractory B-cell precursor ALL. Inotuzumab ozogamicin binds to cancer cells that express the CD22 antigen.

In a randomized trial of 326 patients with relapsed or refractory B-cell ALL who had received 1 or 2 prior treatments, 35.8% of the patients who received inotuzumab ozogamicin experienced complete remission for a median duration of 8.0 months and 17.4% of those who received alternative chemotherapy experienced complete remission for a median duration of 4.9 months)

Common side effects include thrombocytopenia, neutropenia, leukopenia, infection, anemia, fatigue, hemorrhage, pyrexia, nausea, headache, febrile neutropenia, elevated liver function tests, abdominal pain, and hyperbilirubinemia. Severe side effects include hepatotoxicity, myelosuppression, infusion-related reactions, and QT-interval prolongation.

Other Recent Approvals

- On September 14, the FDA approved copanlisib (Aliqopa, Bayer), a phosphoinositide 3-kinase inhibitor, for adults with relapsed follicular lymphoma who have received at least 2 prior lines of treatment.
- Also on September 14, the FDA approved bevacizumab-awwb (Mvasi, Amgen) as a biosimilar to bevacizumab (Avastin, Genentech). The agent, which is used in adults with certain colorectal, lung, brain, kidney, and cervical cancers, is the first oncology biosimilar to receive FDA approval.