By Devon Schuyler

Axicabtagene, Second CAR T-Cell Therapy, Approved in Lymphoma

The US Food and Drug Administration (FDA) approved the T-cell therapy axicabtagene ciloleucel (Yescarta, Kite) on October 18 for use in adults with certain forms of relapsed or refractory large B-cell lymphoma who have received at least 2 other kinds of treatment.

Axicabtagene, a chimeric antigen receptor (CAR) T-cell therapy, is the second gene therapy product to receive FDA approval. Indications include diffuse large B-cell lymphoma (DLBCL), primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. The treatment is made by genetically modifying a patient's T cells.

Approval of axicabtagene was based on the results of a single-arm, multicenter clinical trial of 101 adults with relapsed or refractory aggressive B-cell non-Hodgkin lymphoma. The agent produced a complete remission rate of 51%; the median duration of response was 9.2 months.

The labeling for axicabtagene includes a boxed warning for cytokine release syndrome and neurologic toxicities, both of which can be life-threatening. Because of these risks, the FDA is requiring institutions that provide treatment with axicabtagene to be specially certified. Other side effects of axicabtagene include serious infections, prolonged cytopenia, and a weakened immune system.

The FDA is also requiring the drug's manufacturer to conduct a postmarketing observational study to further evaluate long-term safety.

Axicabtagene was approved as an orphan drug after being granted priority review and a breakthrough therapy designation. It has been priced at $373,000.

FDA Approves Acalabrutinib for Mantle Cell Lymphoma

The FDA approved acalabrutinib (Calquence, AstraZeneca) on October 31 for use in adults with mantle cell lymphoma who have received at least 1 prior therapy. Acalabrutinib is a second-generation Bruton tyrosine kinase inhibitor.

Approval was based on results from a single-arm trial of 124 patients with mantle cell lymphoma who had received at least 1 prior treatment. The investigators found that 40% of the patients had a complete response and an additional 41% had a partial response.

Common side effects of acalabrutinib include headache, diarrhea, bruising, myalgia, anemia, thrombocytopenia, and neutropenia. Serious side effects include hemorrhage, infections, and atrial fibrillation. Second primary malignancies may occur.

Acalabrutinib received priority review as well as breakthrough therapy and orphan drug designations. The wholesale acquisition cost will be $14,259 per month.

Letermovir Approved to Prevent CMV Infection After Stem Cell Transplant

The FDA approved oral and intravenous letermovir (Prevymis, Merck) on November 9 for prophylaxis of cytomegalovirus (CMV) infection in CMV-seropositive adults who have received an allogeneic hematopoietic stem cell transplant (HSCT). Letermovir, a non-nucleoside CMV inhibitor, is the first drug approved for this indication.

Approval was based on a phase 3 clinical trial of 495 patients in which those who received letermovir were significantly less likely than those who received placebo to have clinically significant CMV infection, discontinue treatment, or have missing data at week 24 following HSCT (38% vs 61%, respectively). All-cause mortality also was lower with letermovir than with placebo (12% vs 17%, respectively) at week 24 after transplant. The rates of bone marrow suppression were comparable between the letermovir group and the placebo group. The median time to engraftment was 19 days in the letermovir group and 18 days in the placebo group.

Potential adverse events include tachycardia and other cardiac events, nausea, vomiting, diarrhea, peripheral edema, cough, headache, fatigue, and abdominal pain. Nausea was the most frequently reported adverse event that led to discontinuation of letermovir.

Letermovir is contraindicated in patients receiving pimozide or ergot alkaloids, and in patients taking pitavastatin or simvastatin in combination with cyclosporine. It is expected to be available in December at a wholesale acquisition cost of $195 per day for the tablets and $270 per day for the injections.

Other Recent Approvals

- On November 10, the FDA expanded the indication for dasatinib (Sprycel, Bristol-Myers Squibb) tablets to include the treatment of children with Philadelphia chromosome–positive chronic myeloid leukemia in chronic phase.
- On November 16, the FDA approved emicizumab-kxwh (Hemlibra, Roche) to prevent or reduce the frequency of bleeding episodes in children and adults with hemophilia A with factor VIII inhibitors.