

## Tagraxofusp-erzs Approved in Blastic Plasmacytoid Dendritic Cell Neoplasm

The US Food and Drug Administration (FDA) approved tagraxofusp-erzs (Elzonris, Stemline) on December 21 for blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and in children 2 years of age and older. Tagraxofusp-erzs is the first treatment approved for BPDCN and the first approved CD123-targeted therapy.

Approval was based on an open-label, single-arm clinical trial, STML-401-0114 (NCT02113982), in which patients with untreated or relapsed/refractory BPDCN received intravenous tagraxofusp-erzs at a dose of 12 µg/kg. Among 13 patients with untreated BPDCN, a complete response or clinical complete response occurred in 7 patients after a median follow-up of 11.5 months. Among 15 patients with relapsed/refractory disease, a complete response occurred in 1 patient (duration, 111 days) and a clinical complete response occurred in 1 patient (duration, 424 days).

The most common adverse reactions, affecting at least 30% of the patients, were capillary leak syndrome, nausea, fatigue, peripheral edema, pyrexia, and weight increase. The most common laboratory abnormalities were decreases in albumin, platelets, hemoglobin, calcium, and sodium, and increases in glucose, alanine transaminase, and aspartate transaminase.

Tagraxofusp-erzs received priority review, breakthrough therapy designation, and orphan drug designation.

## FDA Approves Ravulizumab for Paroxysmal Nocturnal Hemoglobinuria

The FDA approved ravulizumab (Ultomiris, Alexion) on December 21 for the treatment of paroxysmal nocturnal hemoglobinuria (PNH). Ravulizumab is a long-acting complement inhibitor that prevents hemolysis. The agent is injected every 8 weeks, which is notable because the only other approved therapy for PNH requires treatment every 2 weeks.

Approval of ravulizumab was based on 2 clinical trials. In the first trial, 246 patients with treatment-naïve PNH were randomly assigned to receive ravulizumab or eculizumab (Soliris, Alexion), the current standard of care for PNH. In this trial, ravulizumab was noninferior to eculizumab regarding breakthrough hemolysis and avoidance of blood transfusion. In the second trial, 195 patients with PNH who were clinically stable after treatment with eculizumab for at least 6 months were randomly assigned to receive ravulizumab or continue eculizumab. As in the

first trial, ravulizumab was noninferior to eculizumab. Common side effects reported by patients in these trials were headache and upper respiratory infection. The prescribing information for ravulizumab includes a Boxed Warning about the risk for life-threatening meningococcal infections and sepsis.

Ravulizumab received priority review and orphan drug designation.

## Calaspargase Pegol-mknl Approved in Acute Lymphoblastic Leukemia

The FDA approved calaspargase pegol-mknl (Asparlas, Servier) on December 20 as part of a multiagent chemotherapeutic regimen for acute lymphoblastic leukemia (ALL) in children and young adults aged 1 month to 21 years. The interval between doses is longer with calaspargase pegol-mknl, which is an asparagine-specific enzyme, than with other available pegaspargase products.

Approval was based on a demonstration of the achievement and maintenance of nadir serum asparaginase activity above the level of 0.1 U/mL when intravenous calaspargase pegol-mknl was given every 3 weeks at a dose of 2500 U/m<sup>2</sup>. The pharmacokinetics of calaspargase pegol-mknl in combination with multiagent chemotherapy were studied in 124 patients with B-cell ALL.

The most common grade 3 or higher adverse reactions, affecting at least 10% of patients, were elevated transaminases, increased bilirubin, pancreatitis, and clotting abnormalities. In a randomized trial, the safety profile of calaspargase pegol-mknl administered every 3 weeks was similar to that of pegaspargase administered every 2 weeks.

## Additional Approvals

- On November 28, the FDA approved gilteritinib (Xospata, Astellas) for the treatment of acute myeloid leukemia with a *FLT3* mutation.
- On November 26, the FDA approved larotrectinib (Vitrakvi, Loxo) for the treatment of solid tumors with a neurotrophic receptor tyrosine kinase (NTRK) gene fusion.
- On November 21, the FDA approved glasdegib (Daurismo, Pfizer) for the treatment of newly diagnosed acute myeloid leukemia in adults 75 years of age or older.
- On November 2, the FDA approved lorlatinib (Lorbrena, Pfizer) for the treatment of ALK-positive metastatic non-small cell lung cancer.