Elzonris™ (tagraxofusp-erzs) – New orphan drug approval

- On December 21, 2018, the FDA announced the approval of Stemline Therapeutics' Elzonris (tagraxofusp-erzs), for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and in pediatric patients 2 years and older.

- BPDCN is an aggressive and rare disease of the bone marrow and blood that can affect multiple organs, including the lymph nodes and the skin. It often presents as leukemia or evolves into acute leukemia.

    - Prior to this approval, there had been no FDA approved therapies for BPDCN. The standard of care has been intensive chemotherapy followed by bone marrow transplantation.

- Elzonris is a CD123-directed cytotoxin composed of recombinant human interleukin-3 and truncated diphtheria toxin fusion protein that inhibits protein synthesis and causes cell death in CD123-expressing cells.

- The efficacy of Elzonris was evaluated in two cohorts of patients in a single-arm clinical study. The first cohort enrolled 13 untreated patients with BPDCN and the second cohort included 15 patients with relapsed or refractory BPDCN. Patients received Elzonris on days 1 to 5 of each 21-day cycle. The efficacy was based on the rate of complete response or clinical complete response (CR/CRc).

    - In the first cohort, CR/CRc was achieved in 7 patients (53.8%; 95% CI: 25.1, 80.8). The median duration of CR/CRc was not reached (range: 3.9 to 12.2 months).
    - In the second cohort, one patient achieved a CR (duration: 111 days) and one patient achieved a CRc (duration: 424 days).

- Elzonris carries a boxed warning for capillary leak syndrome.

- Additional warnings and precautions of Elzonris use include hypersensitivity and hepatotoxicity.

- The most common adverse reactions (≥ 30%) with Elzonris use were capillary leak syndrome, nausea, fatigue, peripheral edema, pyrexia and weight increase. The most common laboratory abnormalities (≥ 50%) were decreases in albumin, platelets, hemoglobin, calcium, and sodium, and increases in glucose, alanine aminotransferase (ALT) and aspartate aminotransferase (AST).

- The recommended dosage of Elzonris is 12 mcg/kg intravenously over 15 minutes once daily on days 1 to 5 of a 21-day cycle. The dosing period may be extended for dose delays up to day 10 of the cycle. Treatment should be continued until disease progression or unacceptable toxicity.

    - Patients should be premedicated with an H_1-histamine antagonist, acetaminophen, corticosteroid, and H_2-histamine antagonist prior to each Elzonris infusion.
    - The first cycle of Elzonris should be administered in the inpatient setting. Subsequent cycles of Elzonris can be administered in the inpatient setting or in a suitable outpatient ambulatory care setting that is equipped with appropriate monitoring for patients with hematopoietic malignancies undergoing treatment.

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- Stemline Therapeutics plans to launch Elzonris in early 2019. Elzonris will be available as a 1,000 mcg/mL single dose vial for injection.