Zynlonta™ (loncastuximab tesirine-lpyl) – New drug approval

- On April 23, 2021 - ADC Therapeutics announced the FDA approval of Zynlonta (loncastuximab tesirine-lpyl), for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low grade lymphoma, and high-grade B-cell lymphoma.
    - This indication is approved under accelerated approval based on overall response rate (ORR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).
- DLBCL, the most common type of non-Hodgkin lymphoma in the U.S., is a rapidly progressing, aggressive disease that is heterogeneous with multiple subtypes.
- Zynlonta is an antibody-drug conjugate targeting CD19. The monoclonal antibody component binds to human CD19, a protein expressed on the surface of cells of B-lineage origin. The small molecule component is SG3199, a cytotoxic alkylating agent.
- The efficacy of Zynlonta was established in LOTIS-2, an open-label, single-arm study in 145 adult patients with relapsed or refractory DLBCL after at least 2 prior systemic regimens. Efficacy was established on the basis of ORR.
    - The ORR was 48.3% (95% CI: 39.9, 56.7).
    - The median duration of response was 10.3 months (95% CI: 6.9, not estimable).
- Warnings and precautions for Zynlonta include effusion and edema, myelosuppression, infections, cutaneous reactions, and embryo-fetal toxicity.
- The most common adverse reactions (≥ 20%) with Zynlonta use, including laboratory abnormalities, were thrombocytopenia, increased gamma-glutamyltransferase, neutropenia, anemia, hyperglycemia, transaminase elevation, fatigue, hypoalbuminemia, rash, edema, nausea, and musculoskeletal pain.
- The recommended dose of Zynlonta is 0.15 mg/kg via intravenous infusion on day 1 every 3 weeks for 2 cycles followed by 0.075 mg/kg every 3 weeks for subsequent cycles.
    - Unless contraindicated, dexamethasone 4 mg orally or intravenously twice daily should be administered for 3 days beginning the day before administering Zynlonta. If dexamethasone administration does not begin the day before Zynlonta, dexamethasone should begin at least 2 hours prior to administration of Zynlonta.
- ADC Therapeutics plans to launch Zynlonta shortly. Zynlonta will be available as a 10 mg lyophilized powder in a single-dose vial for reconstitution and further dilution.