ZYNLONTA® (Loncastuximab tesirine-lpyl) - Premedication

Summary

- ZYNLONTA is a CD19 targeted antibody drug conjugate (ADC) which consists of a monoclonal IgG1 kappa antibody component and a small molecule component (SG3199) which is a pyrrolobenzodiazepine (PBD) dimer and alkylating agent.[2]
- Unless contraindicated, dexamethasone should be administered 4 mg orally or intravenously twice daily 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.[2]
- The rationale for the administration of dexamethasone premedication with ZYNLONTA treatment is based on the Phase 2 clinical trial also referred to as LOTIS-2. To reduce PBD related dimer adverse events (i.e. edema, effusion), patients received premedication with dexamethasone 4 mg orally twice daily the day before ZYNLONTA if possible, the day of ZYNLONTA administration (given at least 2 hours prior to administration when not given the day before; otherwise, any time prior to administration), and the day after ZYNLONTA administration.[3,4]
- ADC Therapeutics does not have data on alternative premedication regimens and does not make recommendations outside of what is stated in the Prescribing Information.[1] If premedication with dexamethasone is not administered according to the recommendations within the ZYNLONTA prescribing information, alternative dosing regimens, are at the clinical discretion of the practitioner. See Relevant Prescribing Information for additional information.

Background

- ZYNLONTA is a CD19-targeted ADC. The monoclonal IgG1 kappa antibody component binds to human CD19, a transmembrane protein expressed on the surface of cells of B-lineage origin. The small molecule component is SG3199, a PBD dimer and alkylating agent.[2]
- Upon binding to CD19, ZYNLONTA is internalized followed by release of SG3199 via proteolytic cleavage. The released SG3199 binds to the DNA minor groove and forms highly cytotoxic DNA interstrand crosslinks, subsequently inducing cell death. ZYNLONTA had anticancer activity in animal models of lymphoma.[2]
- In another study investigating a synthetic PBD dimer SJG-136 (different than the SG3199 PBD dimer in ZYNLONTA), the severity of drug limiting toxicities (DLTs) such as edema, fatigue, dyspnea, and elevations in liver transaminases and alkaline phosphatase were managed in part by steroid (dexamethasone) premedication.[3]
    - Dexamethasone was administered the day prior (Day -1) and through Day 3 of SJG-136 treatment
- Patients in the clinical trials were administered premedication with dexamethasone to reduce the incidence of PBD related adverse events such as edema or effusion.[3,4]

Clinical Data

- In the LOTIS-2 Phase 2 clinical trial, unless contraindicated, dexamethasone (4 mg orally) was administered twice daily the day before ZYNLONTA administration (if possible), the day of ZYNLONTA administration (given at least 2 hours prior to administration when not given the day before; otherwise, any time prior to administration), and the day after ZYNLONTA administration.[3]

Alternative Premedication Regimen

- If the patient is not administered dexamethasone in the manner recommended within the prescribing information, it is up to the clinical judgment of the practitioner to administer dexamethasone in a manner which may help to reduce any PBD related adverse events.

Literature Search

- A PubMed biomedical literature search conducted on August 26, 2024, yielded no relevant data regarding alternative steroid premedication regimens while on ZYNLONTA treatment.

Relevant Prescribing Information

Section 2: Dosage and Administration[2]

2.2: Recommended Premedication

- Unless contraindicated, administer dexamethasone 4 mg orally or intravenously twice daily 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.

References

[1] Data on File, Premedication Memo. ADC Therapeutics.
[2] ZYNLONTA® (loncastuximab tesirine-lpyl) for injection Prescribing Information, October 2022.
[3] Data on File, LOTIS-2 Clinical Study Report. ADC Therapeutics.
[4] Puzanov I, Lee W, Chen AP, et al. Phase 1 pharmacokinetic and pharmacodynamic study of SJG-136, a novel DNA sequence selective minor groove cross-linking agent, in advanced solid tumors. *Clin Cancer Res.* 2011; 17:11(3794-3802).