ZYNLONTA® (loncastuximab tesirine-lpyl) – Use in Patients with p53 Mutation

Overview

- The p53 protein mediates cell-cycle arrest when cells experience stressful challenges such as DNA damage, hypoxia, or oncogene activation, whereas mutant p53 protein results in cell-cycle dysregulation, genomic instability, and uncontrolled proliferation of damaged cells.[1]
    - Mutations in p53 occur with a frequency of 5% (myelodysplastic syndromes) to 50% (acute lymphoblastic leukemia–L3 type) and have been reported in various hematologic malignancies. In most of these cases, a mutated p53 protein has been associated with advanced disease or with the development of resistance to therapy.[2]
    - p53 mutation and/or expression has a negative influence on survival and therefore can serve as a prognostic indicator.[2]
- ADC Therapeutics did not test for p53 mutations in the LOTIS-1 and LOTIS-2 studies.[3]

Literature Search

- A PubMed biomedical literature search conducted on April 16, 2025, yielded no relevant data regarding the use of ZYNLONTA in patients with a p53 mutation.

Prescribing Information

Section 1: Indications and Usage[4]

- ZYNLONTA is indicated 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 [see Clinical Studies (14.1)]. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Section 14: Clinical Studies[4]

Section 14:1 Relapsed or Refractory Diffuse Large B-cell Lymphoma.

- The efficacy of ZYNLONTA was evaluated in LOTIS-2 (NCT03589469), an open-label, single-arm trial in 145 adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after at least 2 prior systemic regimens. The trial excluded patients with bulky disease and active central nervous system lymphoma.
- Of the 145 patients enrolled, the median age was 66 years (range 23 to 94), 59% male, and 94% had an ECOG performance status of 0 to 1. Race was reported in 97% of patients; of these patients, 90% were White, 3% were Black, and 2% were Asian. The diagnosis was DLBCL not otherwise specified (NOS) in 88% (including 20% with DLBCL arising from low-grade lymphoma) and high-grade B-cell lymphoma in 7%. The median number of prior therapies was 3 (range 2 to 7), 63% with refractory disease, 17% with prior stem cell transplant, and 9% with prior chimeric antigen receptor (CAR) T-cell therapy.

References

[1] Young KH, Leroy K, Møller MB, et al. Structural profiles of TP53 gene mutations predict clinical outcome in diffuse large B-cell lymphoma: an international collaborative study. *Blood*. 2008;112(8):3088-3098. doi:10.1182/blood-2008-01-129783.
[2] Koduru PR, Raju K, Vadmal V, et al. Correlation between mutation in P53, p53 expression, cytogenetics, histologic type, and survival in patients with B-cell non-Hodgkin's lymphoma. *Blood*. 1997;90(10):4078-4091.
[3] Data on File, p53 Mutation Memo. ADC Therapeutics.
[4] ZYNLONTA® (loncastuximab tesirine-lpyl) FDA-approved Prescribing Information. October 2022.

ADC Therapeutics encourages all health care professionals to report any adverse events and product quality complaints to medical information at 855-690-0340. Please consult the ZYNLONTA Prescribing Information.