Loncastuximab tesirine-lpyl (ZYNLONTA®) – National Comprehensive Cancer Network® (NCCN®) Recommendations

Summary

- ZYNLONTA is a CD19-directed antibody and alkylating agent conjugate indicated for the treatment of adult patients with relapsed or refractory (R/R) 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.[1]
    - This indication is approved under accelerated approval based on overall response rate.
    - Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend loncastuximab tesirine (ZYNLONTA) as an NCCN Category 2A recommended treatment option for selected subtypes of B-cell lymphomas.[2] A Category 2A recommendation is defined as follows by National Comprehensive Cancer Network® (NCCN®): Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.[2]
- The NCCN Guidelines® recommend loncastuximab tesirine + rituximab as a Category 2B recommended treatment option for selected subtypes of B-cell lymphomas.[2] A Category 2B recommendation is defined as follows: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- Details regarding the NCCN recommendations for loncastuximab tesirine (ZYNLONTA) are provided below. Please note the information contained in this letter is current as of date and is subject to change with the changing treatment landscape.

Background

- ZYNLONTA is a CD19-directed antibody and alkylating agent conjugate 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.[1]
    - This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).
- ZYNLONTA should be administered as an intravenous (IV) infusion administered over 30 minutes on Day 1 of each cycle (every 3 weeks). The recommended dosage is as follows:[1]
    - 0.15 mg/kg every 3 weeks for 2 cycles, followed by 0.075 mg/kg every 3 weeks for subsequent cycles.

NCCN Recommendations

Classic Follicular Lymphoma[2]

- Third line and subsequent therapy "-" Other Recommended regimens
    - Loncastuximab tesirine + rituximab is an option (only after ≥2 lines of systemic therapy) (**2B recommendation**)
    - It is unclear if loncastuximab tesirine or if any other CD19–directed therapy would have a negative impact on the efficacy of subsequent anti-CD19 CAR T-cell therapy.

- Loncastuximab tesirine is FDA approved for relapsed or refractory DLBCL, high-grade B-cell lymphoma (HGBL) with translocation of MYC and BCL2 and/or BCL6 (double-/triple-hit lymphoma), and HGBL, NOS, as well as DLBCL arising from FL and MZL.

Diffuse Large B-Cell Lymphoma[2]

- Third line and subsequent therapy "-" Other Recommended regimens
  - Loncastuximab tesirine is an option (only after ≥2 lines of systemic therapy) (**2A recommendation**)
  - It is unclear if loncastuximab tesirine or if any other CD-19 directed therapy would have a negative impact on the efficacy of subsequent anti-CD19 CAR T-cell therapy.
  - Loncastuximab tesirine is FDA approved for relapsed or refractory DLBCL, high-grade B-cell lymphoma (HGBL) with translocation of MYC and BCL2 and/or BCL6 (double-/triple-hit lymphoma), and HGBL, NOS, as well as DLBCL arising from FL and MZL.

Follicular Lymphoma and Nodal Marginal Zone Lymphoma[2]

- Histologic transformation of follicular lymphoma (FL) to DLBCL and histologic transformation of nodal marginal zone lymphoma (MZL) to DLBCL after multiple lines of prior therapies
- Other recommended regimens.
  - Loncastuximab tesirine (only after ≥2 lines of systemic therapy) (**2A recommendation**)
  - Loncastuximab tesirine is an appropriate option for patients with no intention to proceed to transplant.
  - It is unclear if loncastuximab tesirine or if any other CD19–directed therapy would have a negative impact on the efficacy of subsequent anti-CD19 CAR T-cell therapy.
  - Loncastuximab tesirine is FDA approved for relapsed or refractory DLBCL, high-grade B-cell lymphoma (HGBL) with translocation of MYC and BCL2 and/or BCL6 (double-/triple-hit lymphoma), and HGBL, NOS, as well as DLBCL arising from FL and MZL.

References

[1] ZYNLONTA® (loncastuximab tesirine-lpyl) for injection Prescribing Information, October 2022.
[2] Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas V.2.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed February 25, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org

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.