Patients with refractory or relapsed diffuse large B-cell lymphoma (R/R DLBCL) typically have poor outcomes following treatment. The evaluation of loncastuximab tesirine (Lonca), a novel anti-CD19 monoclonal antibody conjugated to a pyrrolobenzodiazepine (PBD) dimer toxin, indicated for the treatment of R/R DLBCL, is discussed in this context. Lonca is a bispecific antibody expressing a hingeless anti-CD19 monovalent arm and a PBD-conjugated anti-CD37 bispecific arm, which mediates the death of tumor cells by engaging T cells.

### Methods

**Study design**

This is a phase 3, randomized, open-label, two-part, two-arm, multicenter study testing loncastuximab tesirine (Lonca-R) plus rituximab in patients with R/R DLBCL.

**Study assessments**

- **Patient selection**: Eligible patients were adults with histologically confirmed R/R DLBCL, including those with prior autologous hematopoietic cell transplantation, and measurable disease per the 2014 Lugano criteria.

### Key inclusion criteria

- patients with R/R DLBCL in a nonrandomized safety run-in period (part 1)
- patients with R/R disease following at least one multiagent combination therapy
- Refractory or relapsed diffuse large B-cell lymphoma (R/R DLBCL)
- Measurable disease (2014 Lugano Classification)
- Key secondary endpoints include overall survival, overall response rate, safety, duration of response, changes in PROs from baseline.

### Key exclusion criteria

- active infection requiring drainage or pleural effusion either requiring drainage or treatment with antibiotics at study entry
- positive serologic evidence of HCV infection without completion of anti-viral treatment
- current or prior malignancies requiring specific therapeutic intervention
- other active malignancies
- concomitant therapies not allowed
- inability to provide informed consent

### Results

- 19 (95%) patients had at least 1 treatment-emergent adverse event (TEAE), and 10 (50%) patients had grade ≥3 TEAEs
- Lonca-R demonstrated no new safety signals and showed encouraging antitumor activity in patients with R/R DLBCL.

### Conclusions

The results from the LOTIS-5 trial demonstrate the potential of loncastuximab tesirine in patients with R/R DLBCL, providing a new therapeutic option in this challenging disease setting.

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**References**

- [6] Employee for US Oncology; research funding from ADC Therapeutics, BeiGene, Daiichi Sankyo, and Janssen.
- [8] Employee of ADC Therapeutics with stock ownership.
- [9] Employee of ADC Therapeutics with stock ownership.