LONCASTUXIMAB TESIRINE IN R/R DLBCL: A SYSTEMATIC REVIEW AND META-ANALYSIS

Abat Khan, MD[1]*; Hira Habib, MD[2]; Ayesha Imran Butt, MBBS[2]; Haneen Kamran, MBBS[2]; Amna Ahmad, MBBS[2]; Muhammad Husnain, MD[3]; Bilal Khan, MD[4]; Hira Hameed, MBBS[5]; Ahmad Hassan, MBBS[6]; Muhammad Siddique Karimi, MBBS[7]; Fernando Vargas Madueno, MD1; Carlos Silva Rondon, MD1; Jose Sandoval-Sus, MD1

Moffitt Cancer Center at Memorial Healthcare System, Pembroke Pines, FL, USA

Introduction

- Relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL) presents limited treatment options for patients ineligible for stem cell transplantation or CAR T-cell therapy.
- Loncastuximab tesirine is a CD19-directed antibody-drug conjugate showing promising activity as a single agent.
- Limited pooled data exist to evaluate its real-world efficacy and safety.

Aim

- To evaluate the efficacy and safety of loncastuximab tesirine monotherapy in patients with R/R DLBCL through a systematic review and meta-analysis.

Objectives

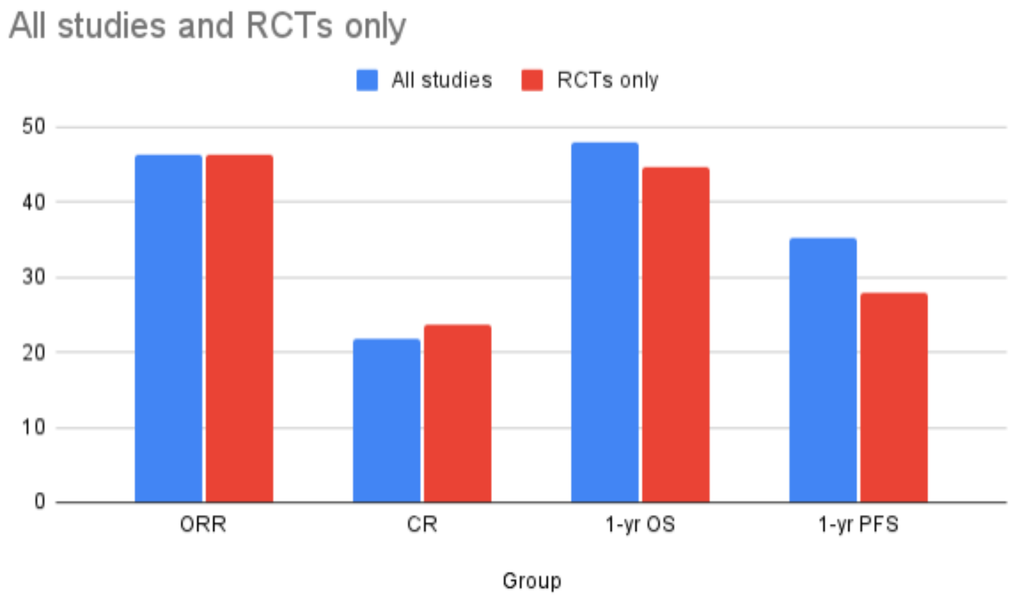
- Determine pooled overall response rate (ORR) & complete response (CR) rate.
- Assess pooled 1-year overall survival (OS) and progression-free survival (PFS).
- Quantify the frequency of hematologic and non-hematologic adverse events.

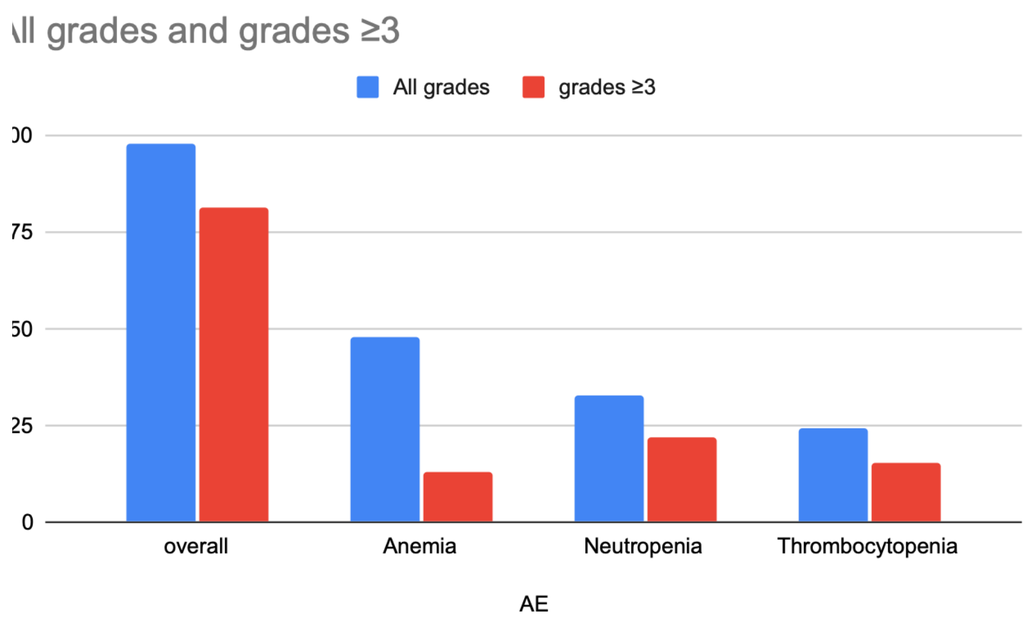
Methods

- Systematic search of PubMed, Embase, and Cochrane CENTRAL through March 2025.
- Inclusion of clinical studies reporting loncastuximab tesirine monotherapy outcomes.
- Data extraction by two independent reviewers.
- Random-effects modeling of absolute risk performed in R (v4.4.3).
- Heterogeneity assessed using the I^2 statistic; publication bias evaluated by Egger's test and funnel plots.

Results

- **Studies included:** 7 (3 randomized controlled trials).
- Total pts: 748, 60.7% males. Median age: 64.9yrs, range 20-79.
- Median line of therapies: 3, range: 0-11
- **Pooled ORR:** 46.3% (95% CI: 35–57)
- **Pooled CR:** 21.9% (95% CI: 17–27)
- **1-year OS:** 48.0% | **1-year PFS:** 35.2%
- In RCT subgroup:
  - ORR: 46.2%, CR: 23.6%
  - 1-year OS: 44.6%, 1-year PFS: 28.0%
- **Adverse Events:**
  - Treatment-emergent AEs: 98%, Grade ≥3 AEs: 81.5%
  - Common hematologic AEs: anemia (47.9%, grade ≥3: 13.1%), neutropenia (32.9%, grade ≥3: 22.0%), thrombocytopenia (24.1%), leukopenia (15.9%)
  - Non-hematologic AEs: hypokalemia (25.8%), peripheral edema (23.5%), rash (19.9%), fatigue (20.1%), fever (15.4%), vomiting (12.4%)





Summary

- Loncastuximab tesirine shows moderate efficacy in heavily pretreated R/R DLBCL with nearly half of patients achieving response.
- Survival outcomes at 1 year remain modest but clinically meaningful given limited alternatives.
- High rates of hematologic toxicity emphasize the need for monitoring and supportive care.

Discussion

- This analysis reinforces loncastuximab tesirine as a viable option for patients ineligible for curative-intent therapies.
- ORR and CR rates are comparable across trial and real-world data.
- Toxicity profile remains significant, particularly hematologic suppression, highlighting a potential role for biomarker-based patient selection.
- Future studies should focus on combinations, mitigation of toxicities, and identification of predictive biomarkers to optimize therapy.

References

1. Caimi PF, Ai WZ, Alderuccio JP, Ardeshna KM, Hamadani M, Hess B, Kahl BS, Radford J, Solh M, Stathis A, Zinzani PL, Wang Y, Qin Y, Wang L, Xu ZC, Carlo-Stella C. Loncastuximab tesirine in relapsed/refractory diffuse large B-cell lymphoma: long-term efficacy and safety from the phase II LOTIS-2 study. Haematologica. 2024 Apr 1;109(4):1184-1193. doi: 10.3324/haematol.2023.283459. PMID: 37646659; PMCID: PMC10985439.
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Contact Email: Abkhan@mhs.net