First Comprehensive Real-World Analysis of CRS/ICANS Management, Escalation Patterns, and Outcomes Across CD3×CD20 Bispecific Antibodies in Lymphoma

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BACKGROUND

CD3×CD20 bispecific antibodies (BsAbs) are reshaping treatment for relapsed/refractory B-cell lymphomas, but real-world recognition, escalation, and management of cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS) remain incompletely standardized.

As BsAbs move earlier in lymphoma care and into broader practice settings, integrated data linking **timing, severity, grade-specific interventions, ICU utilization, toxicity resolution, and adjudicated mortality** across multiple BsAbs remain limited.

STUDY OBJECTIVE

To define CRS/ICANS presentation, management escalation, and clinically consequential outcomes across **glofitamab, epcoritamab, and mosunetuzumab**.

METHODS

- Retrospective, single-center review at Mount Sinai Hospital.
- Adults with lymphoma treated with CD3×CD20 bispecific antibodies from **January 2021 through December 2025**.
- CRS and ICANS graded per **ASTCT criteria**.
- Agent-specific patterns evaluated by exposure using **Fisher's exact test**.
- CRS/ICANS-related mortality adjudicated by **chart review**.

REFERENCES

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3. Thieblemont C, Phillips T, Ghesquieres H, et al. *J Clin Oncol.* 2023;41(12):2238-2247.
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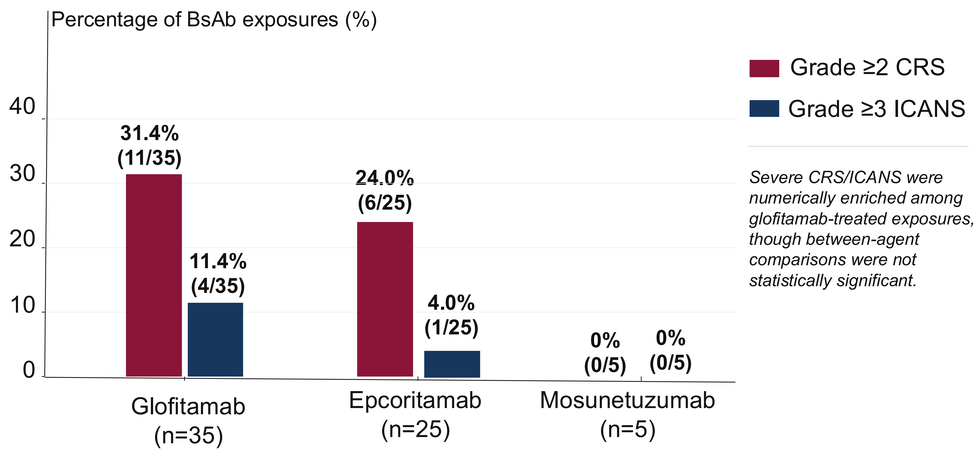
RESULTS

Among **63 patients**, there were **65 BsAb exposures**: 35 glofitamab, 25 epcoritamab, and 5 mosunetuzumab; 2 patients received sequential BsAbs. CRS occurred in **35/63 patients (55.6%)** and was predominantly low-grade, with grade ≥2 CRS in **17/63 (27.0%)**. ICANS occurred in **6/63 patients (9.5%)**, including grade ≥3 ICANS in **5/63 (7.9%)**; **5/6 ICANS cases occurred with concurrent CRS**.

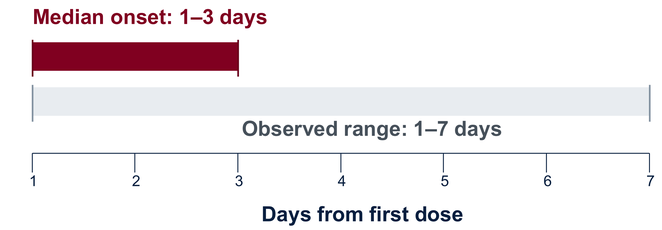
Figure 1. Agent-specific severe CRS and ICANS



Severe CRS/ICANS were numerically enriched among glofitamab-treated exposures, though between-agent comparisons were not statistically significant.

Percentages are calculated per agent exposure. CRS endpoint shown is grade ≥2; ICANS endpoint shown is grade ≥3. Between-agent comparisons were not statistically significant (all p>0.05).

Figure 2. Timing of CRS/ICANS onset after treatment initiation



CRS/ICANS clustered early after treatment initiation.

Figure 3. Management of CRS and ICANS by toxicity severity

Toxicity / severity	Management
Grade 1 CRS (n=18)	Supportive care alone: **10** Tocilizumab: **6** Corticosteroids: **2**
Grade 2 CRS (n=13)	Tocilizumab: **9** Corticosteroids: **11** Combination therapy: **9** Supportive care alone: **2**
Grade 3 CRS (n=4)	Tocilizumab: **4** Most also received corticosteroids
ICANS (n=6)	Corticosteroids: **6** Anakinra: **5**

Management escalation paralleled toxicity severity, with greater use of tocilizumab, corticosteroids, and anakinra for higher-grade events.

Values represent documented interventions by toxicity grade; combination therapy refers to tocilizumab plus corticosteroids.

Figure 4. Clinical outcomes associated with CRS/ICANS

ICU admission	Toxicity resolution	CRS/ICANS-related mortality
14.3% **9/63** required toxicity-related ICU admission	**88.9%** **32/36** patients with CRS and/or ICANS had toxicity resolution	**4.8%** **3/63** Among patients with CRS and/or ICANS **8.3%** **3/36**

ICU admission reflects toxicity-related ICU-level care.

CONCLUSION

- **CRS was common but predominantly low-grade, whereas ICANS was infrequent but clinically consequential.**
- **Severe CRS/ICANS drove ICU utilization and adjudicated mortality, with management escalation paralleling toxicity severity.**
- **The early timing of toxicity supports rapid recognition and standardized severity-based management pathways; potential agent-specific toxicity signals require validation.**