Title: *AKI Following Bispecific T-Cell Engager Therapy in Hematologic Malignancies: A Multicenter Cohort Study*

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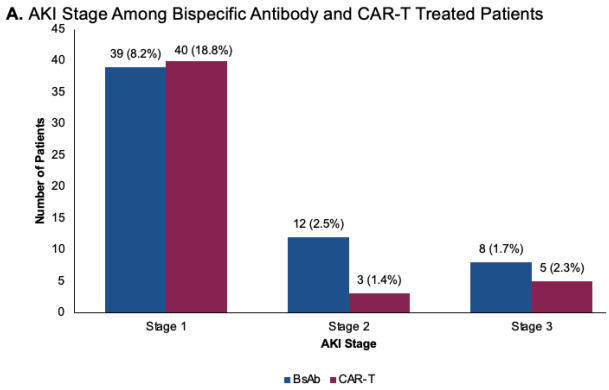
Background: Bispecific antibodies (BsAbs) have transformed the therapeutic landscape for blood cancers, including multiple myeloma (MM) and non-Hodgkin's Lymphomas (NHL), offering highly effective, off-the-shelf immunotherapy options for relapsed and refractory disease. Despite the expanding use of BsAbs in real-world populations, the renal safety profile of BsAbs remains poorly characterized.

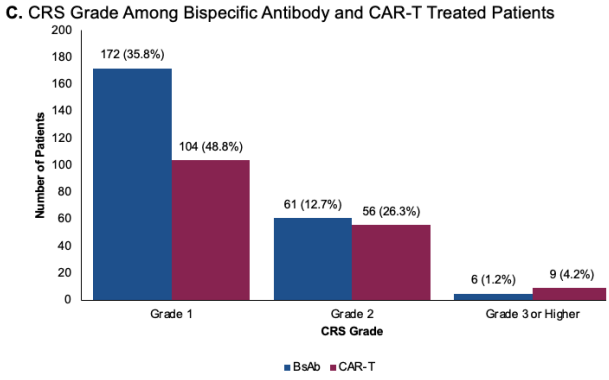
Methods: We retrospectively reviewed all patients with MM and NHL treated with BsAbs across two major academic cancer centers between December 2022 and January 2026. We examined the incidence of a composite outcome of AKI (defined as rise in serum creatinine ≥1.5-fold from pre-BsAb baseline and/or need for renal replacement therapy), or death in the 30 days following the first dose of BsAbs, compared to a contemporaneous control cohort treated with CAR-T. We used multivariable logistic regression to examine risk factors for AKI. We also examined the incidence and severity of cytokine release syndrome (CRS) in the 30 days following treatment initiation.

Results: Of 476 eligible patients who received BsAb, 91 (18.9%) developed the composite outcome of AKI (n=60), death (n=41) or both (n=11). In the CAR-T cohort, of 213 eligible patients, 50 (23.5%) had the composite outcome of AKI (n=48), death(n=4) or both (n=2). AKI severity in each group is shown in Figure 1A. In multivariable analyses, serum albumin <3 g/dL (OR 2.94, 95% CI, 1.35-6.41), platelets <150 K/uL (OR 2.15, 95% CI, 1.15-4), and serum free light chains ≥1000 mg/L (OR 2.99, 95% CI, 1.54-5.83), each assessed at the time of the first dose of BsAbs, were associated with an increased odds of AKI or death (Figure 1B). CRS grade ≥ 2 occurred in 67 (14.9%) patients treated with BsAbs compared to 65 (30.5%) receiving CAR-T (Figure 1C). Patients with AKI after bispecific therapy were more likely to have CRS grade 2 or higher than those without AKI (35 vs. 11%).

Conclusion: We identified key risk factors for AKI in patients treated with BsAbs, and also found that the incidence of AKI or death was lower in this cohort compared to CAR-T -treated patients. Patients with AKI were also more likely to have concurrent CRS. Prospective studies are needed to further evaluate the safety of BsAbs.

Figure 1. Kidney outcomes, risk factors, and cytokine release syndrome following bispecific antibody therapy. **(A)** Severity of acute kidney injury (AKI) among patients treated with bispecific antibodies and CAR-T therapy. **(B)** Multivariable logistic regression identifying risk factors for the composite outcome of AKI or death after bispecific antibody therapy. **(C)** Incidence and severity of cytokine release syndrome (CRS) in patients treated with bispecific antibodies and CAR-T therapy.





B. Risk Factors for AKI Following Bispecific Antibody Treatment in Multivariable Adjusted Model

Variable	OR (95% CI)	Forest Plot	p-value
Age (yrs)	0.98 (0.96–1.01)		0.20
Male sex	1.26 (0.75–2.11)		0.40
eGFR (ml/min/m²)			0.30
≥ 60	REF		
<60	0.62 (0.34–1.13)		
Nephrotoxic drug exposure[a]	1.82 (0.88–3.75)		0.09
Albumin (g/dl)			0.02
≥ 3.5	REF		
3.0-3.4	1.67 (0.87–3.23)		
<3	2.94 (1.35–6.41)		
Hemoglobin (g/dL)			0.40
≥ 10	REF		
<10	1.49 (0.84–2.65)		
Platelets (K/uL)			0.01
≥ 150	REF		
<150	2.15 (1.15–4.00)		
Diabetes mellitus	0.92 (0.51–1.67)		0.80
Hypertension	1.42 (0.78–2.56)		0.20
LDH (U/L)			0.30
<500	REF		
≥500	1.63 (0.86–3.09)		
sFLC (mg/L)			<0.01
<1000	REF		
≥1000	2.99 (1.54–5.83)		

a Nephrotoxic medication exposure included diuretics, ACE inhibitors/ARBs, nonsteroidal anti-inflammatory drugs, intravenous contrast, aminoglycosides, antiviral medications, azole antifungals, and trimethoprim-sulfamethoxazole.