Infection Risk in CAR T vs Bispecific Antibodies in B cell Lymphoma: A Systematic Review and Meta-Analysis

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Introduction

CD3xCD20 bispecific antibody (BsAb) therapy and CD19 directed chimeric antigen receptor (CAR) T cell therapy are novel immunotherapies that have shown impressive efficacy in B cell lymphomas but also come with significant morbidity and mortality, including infections. While BsAbs have lower rates of cytokine release syndrome (CRS) and neurotoxicity, the comparative risk of infections between these two regimens is not fully understood.

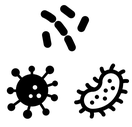
Objectives

This meta-analysis compares rates of infections between commercially approved CAR T and bispecific antibody therapy in patients with B cell lymphomas (B-NHL).

Methods

We conducted a systematic review for prospective trials assessing commercially approved CAR T and BsAbs in patients with B-NHL. We searched MEDLINE, Embase, and Cochrane until January 2025 for prospective trials assessing CAR T and BsAbs in patients with indolent or aggressive B-NHL published on or after 2015 with at least 30 patients.

We used random effects models to evaluate all grade infections, grade 3+ infections, and infection-related mortality, calculating both pooled rates per patient and per patient-month.



Infections are a major cause of morbidity and mortality after both CAR T and BsAbs, but comparative infection rates between the two therapies are unknown.



We assessed all grade infections, grade 3+ infections, and infection-related mortality.



The cumulative effect of continuous dosing of bispecific antibodies may lead to higher risk of infection.

Results

25 studies comprising 3202 patients
Per patient analysis: CAR T vs BsAb
- All-grade (0.44 vs 0.54; p = 0.18)
- Grade 3+ (0.16 vs 0.22; p = 0.08)
- Mortality (0.04 vs 0.03; p = 0.26)

Per patient-month: CAR T vs BsAb
- All-grade (0.0397 vs 0.0167; p = 0.0012)
- Grade 3+ (0.0165 vs 0.0069; p = 0.0003)
- Mortality (0.0023 vs 0.0022, p = 0.96).

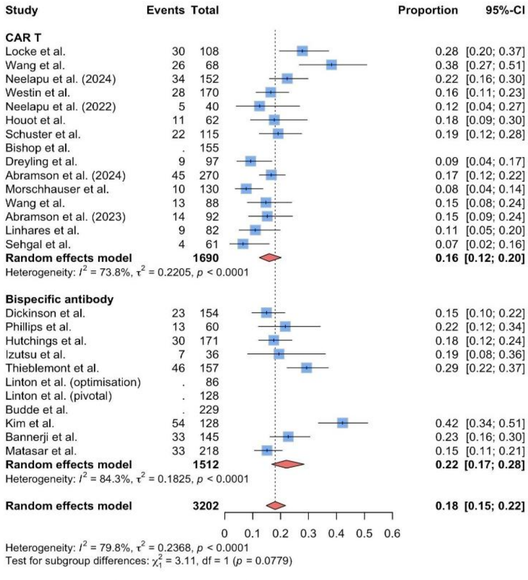


Figure 1: Grade 3+ Infections per patient

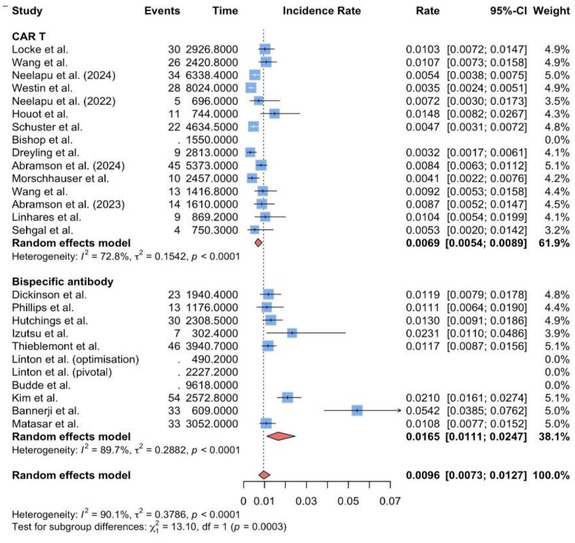


Figure 2: Grade 3+ Infections per patient-month

References

1.CAR T cells vs bispecific antibody as third-or later-line large B-cell lymphoma therapy: a meta-analysis. *Blood*

2. A systematic review and meta-analysis of nonrelapse mortality after CAR T cell therapy. *Nat Med*

3.Infections in patients with lymphoma treated with bispecific antibodies: a systemic review and meta-analysis. *Blood Adv*

Discussion

BsAbs are considered a safer alternative to CAR T therapy for relapsed/refractory lymphoma. Our findings point to an equivalent or sometimes greater infection risk with BsAbs when following patients over time. We believe this may be due to the prolonged and sometimes indefinite administration of BsAbs. Our study highlights the importance of thoroughly capturing infections in the design of clinical trials using either treatment modality.

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