Efficacy and Safety of Bridging Zanubrutinib Regimen with CAR T-Cell Therapy in R/R DLBCL: A Systematic Review and Meta-Analysis

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Introduction

Chimeric antigen receptor (CAR) T-cell therapy has transformed treatment for relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL) by targeting CD-19. However, significant challenges remain, including high relapse rates and limited durable responses. Research suggests that **Bruton's tyrosine kinase (BTK) inhibitors**, such as Zanubrutinib, could enhance the effectiveness of CAR T-cell therapy by modifying the tumor microenvironment and improving T-cell expansion.

Aim

The purpose of this study is to comprehensively assess the therapeutic value and safety of combining Zanubrutinib with CAR T-cell therapy.

Methods

A systematic literature search was conducted across PubMed, Embase, and Cochrane databases. The search identified studies evaluating the outcomes of combined Zanubrutinib and CAR T-cell therapy in patients with R/R DLBCL.

- **Primary outcomes** were the overall response rate (ORR) and complete response (CR) rate.
- **Secondary outcomes** included the percentage of patients achieving progression-free survival (PFS) and overall survival (OS) at the end of follow-up, as well as the incidence of grade 1–2 cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS).

Meta-analyses of pooled proportions were performed using a random-effects model. Statistical heterogeneity was assessed using the I 2 statistic. All analyses were performed in R version 4.4.2

Results

The meta-analysis included five studies with a total of 117 patients.

•The pooled **ORR** was **84%** [95% CI: 0.76–0.90]

•The pooled **complete response rate** was **73%** [95% CI: 0.53–0.90]

•The proportion of patients achieving **PFS** was **61%** [95% CI: 0.51–0.69]

•The proportion of patients achieving **OS** was **79%** [95% CI: 0.66–0.89]

Regarding safety, the incidence of grade 1–2 adverse events was:

•**CRS: 77%** [95% CI: 0.69–0.84]

•**ICANS: 15%** [95% CI: 0.07–0.28]

Figure 1: Overall Response Rate

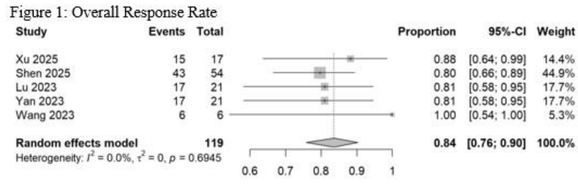


Figure 2: Complete Response Rate

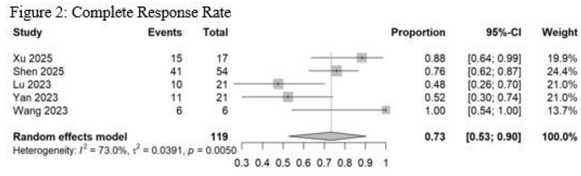


Figure 3: % of population achieving PFS

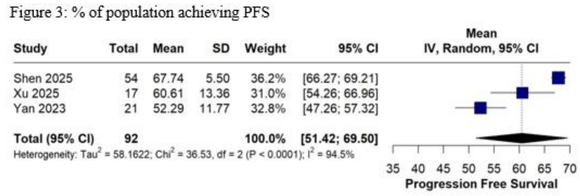


Figure 4: \Overall Survival%

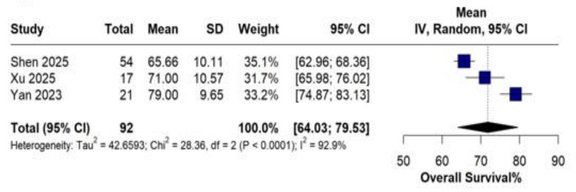


Figure 5: Grade 1-2 CRS

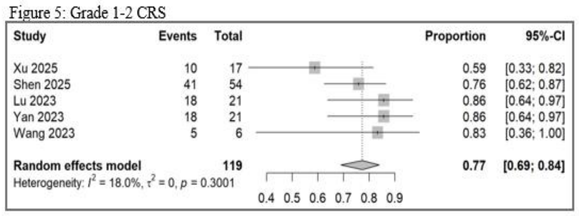
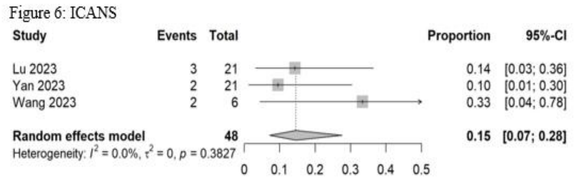


Figure 6: ICANS



Conclusion

Bridging Zanubrutinib regimen in combination with CAR T cell therapy shows promising efficacy with manageable safety profile. Future comparative studies evaluating bridging versus non-bridging therapies are warranted to precisely determine the benefits of bridging therapy.

References

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