SAFETY AND EARLY CLINICAL OUTCOMES OF DUAL-TARGET CD19/CD22 CAR-T STRATEGIES IN RELAPSED/REFRACTORY B-ALL: A SYSTEMATIC REVIEW AND META-ANALYSIS

SOHO ANNUAL MEETING

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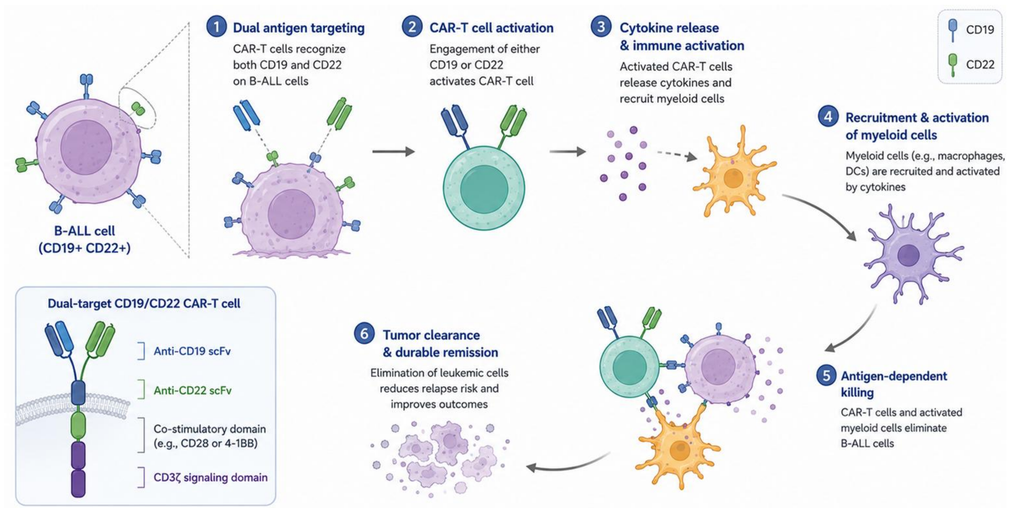
INTRODUCTION

CAR T-cell therapy employs HLA-independent receptors with tumor-targeting scFv and CD3ζ/FcRγ signaling, activating both $CD4^+$ and $CD8^+$ T cells for enhanced anti-tumor effects. Although CD19-directed CARs (Axi-cel, Tisa-cel, Liso-cel) are clinically approved for lymphoma, they carry significant acute toxicities and late risks like secondary malignancies. Since single-agent CAR-T often fails due to antigen escape and evidence on dual-targeting is scarce, our study evaluates the safety and early efficacy of dual-agent CAR-T in ALL..



METHODS

This systematic review and meta-analysis followed PRISMA guidelines. A comprehensive search of PubMed, Scopus, Web of Science, and Cochrane was performed using predefined keywords for dual-targeted (CD19/CD22) CAR-T therapy in relapsed/refractory B-cell acute lymphoblastic leukemia (ALL) across pediatric and young adult populations. After screening 699 initial records and removing duplicates, two independent reviewers selected **14 studies** that met the inclusion criteria (clinical trials enrolling R/R B-ALL patients receiving CD19/CD22 CAR-T, excluding reviews, case reports, preclinical work, and single-target studies). Data extraction covered baseline characteristics, intervention details, and primary/secondary outcomes, while risk of bias was assessed using the MINORS tool. A meta-analysis was conducted using RevMan 5.4, with sensitivity analyses (leave-one-out and subgroup analyses) to assess robustness.

RESULTS

Efficacy

Efficacy Outcomes - Bispecific CAR-T-Cell Studies

Outcome	N studies	Event proportion	95% CI	I2 (%)	P het
Best overall response within 3 months	12	0.94	0.87 - 0.97	0.0	0.711
Best response by day 28	13	0.92	0.84 - 0.96	24.2	0.199
Bone marrow remission by flow cytometry	13	0.91	0.85 - 0.95	0.0	0.843
Bridging to HSCT	13	0.16	0.07 - 0.32	55.2	0.008
CR/CRi rate	14	0.92	0.86 - 0.96	23.0	0.205
MRD-negative CR rate	13	0.90	0.84 - 0.94	0.0	0.834
Overall remission rate	12	0.95	0.87 - 0.98	30.1	0.152
Overall response rate (ORR)	13	0.94	0.87 - 0.97	0.0	0.761

Adverse Event

Remaining AE - Grouped by Clinical Relatedness

Outcome	N studies	Event proportion	95% CI	I2 (%)	P het
HEMATOLOGIC CYTOPENIAS					
Grade 3-4 anemia	5	0.66	0.46 - 0.81	65.6	0.020
Grade 3-4 cytopenia	3	0.95	0.60 - 1.00	0.0	1.000
Grade 3-4 neutropenia	6	0.86	0.44 - 0.98	62.8	0.020
Grade 3-4 thrombocytopenia	7	0.50	0.31 - 0.69	62.4	0.014
OVERALL SEVERE TOXICITY					
Overall grade 3-4 toxicity	5	0.64	0.14 - 0.95	76.4	0.002
ORGAN-SPECIFIC AE					
Cardiac AE	6	0.15	0.06 - 0.31	54.4	0.052
Gastrointestinal AE	5	0.05	0.00 - 0.53	83.7	<0.001
Hepatic AE	4	0.13	0.04 - 0.33	74.3	0.008
Respiratory AE	4	0.16	0.08 - 0.29	45.6	0.138
SYSTEMIC AND SYMPTOM AE					
Headache	5	0.11	0.02 - 0.41	89.5	<0.001
Temperature ≥38 °C (fever)	7	0.90	0.65 - 0.98	80.6	<0.001

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REFERENCES