INPLASY PROTOCOL

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None declared.

Treatment-Related Adverse Events of Chimeric Antigen receptor T-Cell (CAR-T) Cell Therapy in B-cell hematological malignancies in the Pediatric and Young Adult Population: A Systematic Review and Meta-Analysis

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Review question / Objective: **We aimed to review treatment-related adverse events of CAR-T cell therapy in B-cell hematological malignancies in the pediatric and young adult population.**
Condition being studied: **This review focuses on children and young adults with B-cell hematological malignancies treated with chimeric antigen receptor T-cell therapy and who experienced adverse events.**
Eligibility criteria: **1、Cancer therapy clinical trials or research that involve more than three patients. 2、The subjects were children and young adults (0-30 years old) with a definite diagnosis of B-cell hematological malignancies. 3、Published domestic and foreign CAR-T-related clinical trials; 4、Main outcome indicators included adverse reactions.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 July 2022 and was last updated on 07 July 2022 (registration number INPLASY202270034).

INTRODUCTION

Review question / Objective: **We aimed to review treatment-related adverse events of CAR-T cell therapy in B-cell hematological malignancies in the pediatric and young adult population.**

Condition being studied: This review focuses on children and young adults with B-cell hematological malignancies treated with chimeric antigen receptor T-cell therapy and who experienced adverse events.

METHODS

Participant or population: children and young adults with B-cell hematological malignancies.

Intervention: chimeric antigen receptor T-cell therapy.

Comparator: NA.

Study designs to be included: The references of relevant published trials, case reports, and meeting abstracts were included for meta-analysis.

Eligibility criteria: 1、Cancer therapy clinical trials or research that involve more than three patients. 2、The subjects were children and young adults (0-30 years old) with a definite diagnosis of B-cell hematological malignancies. 3、Published domestic and foreign CAR-T-related clinical trials; 4、Main outcome indicators included adverse reactions.

Information sources: Search for relevant publications in Pubmed、Web of Science, Cochrane、Embase、Wan Fang Data, CNKI、Sinomed from inception to 30 June 2022.

Main outcome(s): Identify the comprehensive incidences and severity of CRS、hematologic toxicity and non-hematologic toxicity as well as the potential differences in AEs across a variety of chimeric antigen receptor (CAR) construct types, doses, and CRS classification criteria, and other factors.

Quality assessment / Risk of bias analysis: The quality of the observational studies was assessed using the Newcastle-Ottawa scale, the evaluated items included selection criteria, comparability, and outcome(cohort) or exposure(case-control). The maximum score was 9, and the trial with a score of less than 7 was excluded. The quality of the cross-sectional studies was assessed using the Agency for Healthcare Research and Quality, Eleven items were evaluated with "yes", "no" and" unclear".

Strategy of data synthesis: The meta-analysis was conducted using STATA version 16.0 software. Event rate (ER) with 95% confidence intervals (CIs) were calculated for each outcome. Pooled CRS、hematologic toxicity and non-hematologic toxicity were calculated using fixed- and random-effects models depending on the heterogeneity across the included studies. The between-study heterogeneity was determined by the I2 value, the levels of heterogeneity were defined as low when I2≤25%, moderate when I2 ranges from 25-50%, and high when I2>50%. The fixed-effect model was used when I2≤50%; and the random-effect model was used when I2>50%. Factors that may influence the incidence of severe adverse events were analyzed by univariate meta-regression. $P < 0.05$ was considered a statistically significant difference.

Subgroup analysis: Subgroup analysis was performed by CAR construct type, dose, CRS classification criteria, and other factors.

Sensitivity analysis: Egger's Regression test was used for sensitivity analysis of data, and each article was excluded and analyzed one by one. The change of heterogeneity was observed and the publication bias was evaluated by funnel plot.

Country(ies) involved: China.

Keywords: CAR-T、chimeric antigen receptor-modified T cell therapy, Childhood B-Cell Hematologic Malignancies、Chronic lymphocytic leukemia、Acute

lymphoblastic leukemia, lymphoma、meta analysis.

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