INPLASY

Efficacy and Safety of Rituximab Combined with Chemotherapy Regimen in Children and Adolescents with Mature B-Cell Non-Hodgkin's Lymphoma: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 February 2025 and was last updated on 27 February 2025.

INTRODUCTION

Review question / Objective To evaluate the efficacy and safety of rituximab combined with chemotherapy compared to chemotherapy alone in improving event-free survival, overall survival, complete remission rate, toxic effects, immune reconstitution, and recurrence rate among children and adolescents aged 0-15 years with mature B-cell non-Hodgkin's lymphoma.

Rationale The rationale for this study is driven by the need to improve outcomes for children and adolescents with mature B-cell NHL, the potential benefits of rituximab observed in adult studies, and the necessity to synthesize existing evidence to provide a comprehensive understanding of its efficacy and safety in pediatricpatients.

Condition being studied Mature B-cell non-Hodgkin's lymphoma (NHL) is a type of malignancy that originates from mature B-cells, a subset of white blood cells responsible for producing antibodies as part of the immune system. This condition primarily affects children and adolescents, representing a significant cause of morbidity and mortality in this age group. The disease is characterized by the uncontrolled proliferation of abnormal B-cells, which can lead to the formation of tumors, systemic symptoms such as fever, weight loss, and fatigue, and, if left untreated, progression to more advanced stages. Common subtypes of mature B-cell NHL in pediatric populations include Burkitt lymphoma, diffuse large B-cell lymphoma, and primary mediastinal large B-cell lymphoma. Early diagnosis and effective treatment are crucial to improving outcomes and reducing the risk of relapse or complications.

METHODS

Search strategy The review utilized a comprehensive search strategy across four major electronic databases (PubMed, Embase, Cochrane Library, and Web of Science) with carefully selected search terms related to rituximab, chemotherapy, mature B-cell non-Hodgkin's lymphoma, and pediatric populations. This approach ensured the identification of a broad range of relevant studies to provide a thorough assessment of the efficacy and safety of rituximab in combination with chemotherapy for pediatric patients with mature B-cell NHL.

Participant or population The review addresses participants who are children and adolescents aged 0-15 years with a confirmed diagnosis of mature B-cell non-Hodgkin's lymphoma. This specific population selection ensures that the findings are relevant and applicable to the unique needs of pediatric patients with this malignancy.

Intervention The intervention evaluated in this review is rituximab combined with standard chemotherapy regimens. The goal is to assess its efficacy and safety in improving outcomes for children and adolescents with mature B-cell non-Hodgkin's lymphoma compared to chemotherapy alone.

Comparator The comparative intervention applied to the target population in this review is chemotherapy alone, representing the standard treatment approach for pediatric patients with mature B-cell non-Hodgkin's lymphoma. This comparison allows for a clear assessment of the incremental benefits and risks associated with the addition of rituximab to existing chemotherapy regimens.

Study designs to be included The review includes randomized controlled trials, prospective and retrospective cohort studies, and case series to comprehensively evaluate the efficacy and safety of rituximab combined with chemotherapy in children and adolescents with mature B-cell NHL. This approach ensures a robust and multifaceted assessment of the research question.

Eligibility criteria The additional inclusion and exclusion criteria defined in this review ensure that the studies included are of high quality, relevant to the research question, and provide sufficient data for a comprehensive analysis of the efficacy and safety of rituximab combined with chemotherapy in pediatric patients with mature B-cell NHL.

Information sources The review employs a multi-faceted approach to information gathering, including electronic databases (PubMed, Embase, Cochrane Library, Web of Science), grey literature, trial registers, reference list screening, and direct contact with authors. This comprehensive strategy ensures that the review is based on a thorough and unbiased collection of data, providing a robust assessment of the efficacy and safety of rituximab combined with chemotherapy in pediatric patients with mature B-cell non-Hodgkin's lymphoma.

Main outcome(s) The primary outcomes of this review include event-free survival (EFS), overall survival (OS), and complete remission rate (CR), with secondary outcomes focusing on the incidence of toxic effects, immune reconstitution, and recurrence rate. These outcomes were assessed using hazard ratios, odds ratios, and mean differences, with specific timing intervals to capture both short-term and long-term treatment effects. This comprehensive approach ensures a thorough evaluation of the efficacy and safety of rituximab combined with chemotherapy in pediatric patients with mature B-cell non-Hodgkin's lymphoma.

Additional outcome(s) In addition to the primary and secondary outcomes, the review may also consider quality of life, time to progression, duration of response, long-term follow-up data, patient-reported outcomes, and cost-effectiveness analysis. These additional outcomes provide a more comprehensive assessment of the intervention's impact on pediatric patients with mature B-cell NHL, addressing both clinical and patient-centered aspects of care.

Data management The mechanism used to manage records and data in this review involved a structured approach, including comprehensive searching, deduplication, screening, data extraction, quality assessment, and statistical analysis. This rigorous process ensured that the review was based on high-quality evidence and provided a comprehensive evaluation of the research question.

Quality assessment / Risk of bias analysis The quality assessment and risk of bias analysis in this review were conducted using established tools (Cochrane Risk of Bias Tool and Newcastle-Ottawa Scale) and involved independent review and discrepancy resolution. The findings revealed a mixed quality profile among the included studies, with some demonstrating low risk of bias and others showing moderate to high risk. Despite this variation, the overall quality was deemed

acceptable for the meta-analysis, supported by the consistency and stability of the results. The GRADE system was used to integrate these factors and provide a comprehensive assessment of the quality of evidence.

Strategy of data synthesis The strategy for data synthesis in this review involved a systematic approach, including standardized data extraction, statistical analysis using appropriate effect measures, assessment of heterogeneity, subgroup analysis, sensitivity analysis, and evaluation of publication bias. This comprehensive strategy ensured that the findings were based on robust and reliable evidence, providing a thorough and unbiased assessment of the efficacy and safety of rituximab combined with chemotherapy in pediatric patients with mature B-cell non-Hodgkin's lymphoma.

Subgroup analysis The subgroup analyses in this review assessed the consistency of the findings across different age categories (children and adolescents combined vs. children alone) and study designs (RCTs vs. non-Randomized studies). The results showed significant improvements in event-free survival, overall survival, and complete remission rate across all subgroups, indicating that the benefits of rituximab are consistent and robust across different patient populations and study types. This supports the overall conclusion that the addition of rituximab to chemotherapy significantly improves outcomes in pediatric patients with mature B-cell non-Hodgkin's lymphoma.

Sensitivity analysis The sensitivity analysis conducted in this review assessed the robustness of the findings by excluding high-risk studies, outliers, and small studies, as well as analyzing results separately by study design. The results remained consistent across all sensitivity analyses, indicating that the findings are robust and reliable. This supports the overall conclusion that the addition of rituximab to chemotherapy significantly improves event-free survival, overall survival, and complete remission rates in children and adolescents with mature B-cell non-Hodgkin's lymphoma.

Country(ies) involved China.

Keywords Rituximab; Chemotherapy; Pediatric; Mature B-cell NHL; Efficacy and Safety.

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