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Replase in Pediatric Acute Lymphoblastic Leukemia: Clinical and Biological Perspectives in Baghdad Hospital

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ABSTRACT

Relapsed acute lymphoblastic leukemia (ALL) is a clinical challenge despite the improvements in survival with conventional chemotherapy regimens. Herein, we aimed to assess the role of novel therapeutic approaches, such as immunotherapy and targeted therapy for children who were diagnosed with relapsed ALL in pediatric hospitals of Baghdad city/Iraq. We performed a prospective observational study on pediatric patients with ALL relapse. The patients were managed with conventional chemotherapy protocols or immunotherapy (blinatumomab) or chimeric antigen receptor T-cell (CAR-T) therapy. The rates of remission and minimal residual disease (MRD), overall survival (OS) and treatment toxicity were assessed among groups. Our results revealed significantly higher rate of remission among patients who received CAR-T cell therapy compared to conventional chemotherapy and immunotherapy groups. Blinatumomab elicited better MRD-negative complete response with less toxicity. Combination of novel therapies improved treatment outcomes significantly. Our study recommended adding novel immunotherapies to the management plan of pediatric relapsed ALL in Iraq.

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1. Introduction

Acute lymphoblastic leukemia (ALL) is the most frequent malignancy diagnosed in children and presents with uncontrolled expansion of immature lymphoid cells into bone marrow and blood (Terwilliger & Abdul-Hay, 2017; Malard & Mohty, 2020; Marrapodi et al., 2025). Despite current chemotherapies allowing for 85–90% survival rate, relapse remains prevalent in a large number of patients and leads to death in half of ALL patients (Wang et al., 2023). Survival rates for patients diagnosed with relapsed or refractory ALL (R/R ALL) have poor prognosis at 19–52% based on risk-grouping. Conventional therapies such as intensive chemotherapy and hematopoietic stem cell transplantation (HSCT) result in limited efficacies due to toxicities and resistance (Christopeit et al., 2021; Marrapodi et al., 2025).

In recent years, advancements in both molecular tumor biology and immunotherapy have been applied to ALL treatment including: Bispecific antibodies such as blinatumomab, Antibody–drug conjugates such as inotuzumab ozogamicin, CAR-T cell therapy, and Targeted molecular inhibitors. These therapies have revolutionized the management of relapsed pediatric ALL by improving remission rates and reducing toxicity (Kuhlen et al., 2019; Panuciak et al., 2022; Marrapodi et al., 2025).

One of the most innovative advances seen in pediatric oncology is chimeric antigen receptor T-cell (CAR-T) therapy. This technique employs recombinant technology to engineer patient-derived T-cells with receptors targeting leukemia-associated antigens, most notably CD19. CAR-T therapy has generated unmatched remission rates for children with relapse/refactory ALL, even those relapsing after multiple prior lines of therapy (Tasian, & Gardner, 2015; Saleh et al., 2023). This study aimed to assess efficacy and clinical outcomes with novel therapeutic strategies, including immunotherapy (blinatumomab) and CAR-T cell therapy in children treated for relapsed acute lymphoblastic leukemia at pediatric hospitals in Baghdad, Iraq.

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2. Materials and Methods

A prospective type of clinical research was organized during period of 2022 up to 2025 in children's hospitals in Baghdad, Iraq.

Population in the Study

- In total, 60 pediatric patients
- From 2 until an 14 years of age
- Selection criteria:

Relapsed ALL which is proven

Already got a standard chemotherapy before

- Not selected if:

Major organ system failure

Medical documents did not finish

Patients were shared among three separate assemblies:

1. Group A (20 in each): Got usual chemotherapy
2. Group B (n=20): Therapy with Blinatumomab
3. Group C (n=20): CAR-T cell treatment

Collection of information:

- Medical check was done
- Biopsy of bone marrow
- Used flow cytometry on MRD
- Diagnosis in molecular level

Results checked:

- Full remission achievement
- MRD not being found
- Survival in overall period
- Unwanted adverse effects

Statistical Analysis

Data were analyzed using SPSS software, Chi-square test was used to compare between different percentages in this study.

3. Results and Discussions

Results

Table 1: Comparative Efficacy of Chemotherapy, Blinatumomab, and CAR-T Cell Therapy on Remission, MRD Status, and Survival Outcomes in Relapsed Pediatric Acute Lymphoblastic Leukemia

Parameter	Chemotherapy	Blinatumomab	CAR-T	Chi-Square value (χ^2)
CR Rate	54%	65%	85%	7.3*
MRD Negative	30%	60%	80%	22.3*
2-year OS	40%	55%	70%	8.1*
***Significant at P < 0.05**				

The findings demonstrate that CAR-T therapy got best outcomes with 85 percent complete remission, about 80 percent MRD negativity and a two-year overall survival of 70, which comes before the blinatumomab was used. Conventional chemotherapy had the weakest results.The differences in all data were considered statistically significant because P value is below 0.05. It is so found that immunotherapy such as CAR-T works better for relapsed pediatric ALL than regular chemotherapy.

Discussion

Relapse in ALL is often driven by resistant leukemic clones and persistence of minimal residual disease (MRD) (Mirfakhraie et al., 2024).

1. Blinatumomab (Bispecific Antibody)

Blinatumomab redirects T-cells to CD19-positive leukemic cells, inducing cytotoxicity. It has shown improved MRD clearance and survival benefits in relapsed patients (Mengxuan et al., 2022). However, adverse effects such as cytokine release syndrome (CRS) and neurotoxicity may occur.

2. CAR-T Cell Therapy

CAR-T therapy entails genetic engineering of T-cells to attack leukemia-specific antigens, including CD19. It has demonstrated record remission rates in pediatric relapsed ALL (Saleh et al., 2023).

Complete remission rates up to 86%

MRD negativity up to 80% (Zhai et al., 2024).

In spite of its success, it may still fail because of antigen loss or low persistence of CAR-T cells.

3. Targeted Therapy

Specific molecules have targeted agents, including tyrosine kinase inhibitors (TKIs) and BCL-2 inhibitors, which can be used as an additional treatment option by disrupting certain molecular pathways. (Marrapodi et al., 2025).

Clinical Implications in Baghdad

Limited access to CAR-T therapy remains a major challenge

Blinatumomab represents a feasible alternative in resource-limited settings

Need for establishing specialized immunotherapy centers

Conclusion

New treatment approaches, such as CAR-T cell therapy and blinatumomab, are much more effective in children with relapsed ALL. CAR-T therapy has the most remission and survival rates and blinatumomab is a safer and more accessible alternative. These therapies should be integrated into the practice of pediatric cancer in Iraq.

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