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ORIGINAL RESEARCH

Blinatumomab for Pediatric High-Risk B-Cell Precursor Acute Lymphoblastic Leukemia: Safety, MRD Response and Survival in a Single-Center Retrospective Cohort

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Background: Advances in the treatment of pediatric acute lymphoblastic leukemia (ALL) have significantly improved outcomes, with overall survival rates exceeding 90%. Despite these favorable results, relapse and resistance to therapy remain major clinical challenges, and ALL is still the second leading cause of cancer-related mortality in children, after central nervous system tumors. The development of immunotherapy has led to new treatment options, including blinatumomab. The aim of this study was to assess the efficacy of blinatumomab treatment and to evaluate its safety profile in pediatric patients with high-risk precursor B-cell ALL.

Material and Methods: We conducted a retrospective single-center cohort study including 13 pediatric patients with high-risk BCP-ALL treated with blinatumomab between 2017 and 2025 in Lublin, Poland. Primary outcomes were MRD negativity and overall survival. Safety was assessed using CTCAE criteria.

Results: MRD positivity before treatment was present in 8/13 patients. After the first cycle, 62.5% achieved MRD negativity, increasing to 75.0% overall after two cycles. Kaplan-Meier estimated 12-month OS was 83.3%, and 24-month OS was 64.8%. Adverse events occurred in 69.2% of patients; grade 3 toxicity in 23.1%. No life-threatening toxicity occurred.

Conclusions: In this small retrospective cohort, blinatumomab demonstrated encouraging MRD response, favorable survival estimates, and acceptable tolerability in pediatric high-risk BCP-ALL. Larger prospective multicenter studies are warranted.

Keywords: blinatumomab, immunotherapy, pediatric, acute lymphoblastic leukemia, bispecific antibody

Introduction

Acute lymphoblastic leukemia (ALL) is the most common malignant neoplasm in the pediatric population.[1] Thanks to advances in understanding the heterogeneous biological basis of ALL, an improvement in overall survival (OS) has been observed in recent years, exceeding 90%. This improvement is largely related to the gradual reduction in the use of intensive chemotherapy in favor of modern targeted therapies.[2] Despite this progress, ALL remains the second most common cause of cancer-related mortality in children, after tumors of the central nervous system, and relapsed leukemia continues to represent a significant therapeutic challenge.[3,4] In the treatment of relapsed and refractory ALL, targeted therapies are playing an increasingly important role, including chimeric antigen receptor T-cell (CAR-T) therapy, antibody–drug conjugates, and bispecific antibodies such as blinatumomab.[2]

Blinatumomab is a bispecific monoclonal antibody of the BiTE (bispecific T-cell engager) class that targets CD3 and CD19 antigens. It consists of two recombinant single-chain variable fragments, which enable binding to CD3-positive T lymphocytes and CD19-positive B lymphocytes. Close interaction between these cells leads to T-cell activation, followed by destruction of malignant cells through mechanisms dependent on the release of cytotoxic substances.[5] In the pediatric

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population, blinatumomab is indicated for patients aged ≥1 year with precursor B-cell acute lymphoblastic leukemia, Philadelphia chromosome-negative, with CD19 expression, whose disease is refractory to treatment or has relapsed after at least two prior lines of therapy, or has relapsed after previous allogeneic hematopoietic stem cell transplantation.[6] According to recent reports from the American Society of Hematology, the addition of blinatumomab to chemotherapy improves event-free survival and overall survival, particularly in intermediate- and high-risk patient groups.[7,8]

Increasing evidence suggests that host-related factors, including nutritional status, may influence treatment tolerance and outcomes in pediatric acute lymphoblastic leukemia. However, data regarding their impact during blinatumomab therapy remain limited.

Therefore, the aim of this study was to evaluate the real-world efficacy and safety of blinatumomab in pediatric patients with high-risk B-cell precursor acute lymphoblastic leukemia treated in routine clinical practice. Specifically, we assessed MRD response, overall survival, relapse occurrence, and treatment-related toxicity.

We hypothesized that blinatumomab would be associated with meaningful MRD clearance and acceptable tolerability in this real-world cohort.

Materials and Methods

Study Design and Setting

This study was a retrospective, single-center, observational cohort study conducted at the Department of Pediatric Hematology, Oncology and Transplantology, University Children's Hospital in Lublin, Poland. The study evaluated consecutive pediatric patients treated with blinatumomab between January 2017 and November 2025.

Medical records were reviewed between September and November 2025, and data analysis was completed in December 2025.

The manuscript was prepared in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations for cohort studies.

Participants and Eligibility Criteria

Eligible participants were patients younger than 18 years of age with a confirmed diagnosis of B-cell precursor acute lymphoblastic leukemia (BCP-ALL) who received at least one cycle of blinatumomab during the study period.
Patients were treated with blinatumomab in one of two predefined clinical settings:

- Frontline high-risk setting – patients with an inadequate response to induction therapy who were subsequently classified as high risk according to contemporary treatment protocols.
- Relapsed disease setting – patients with relapsed ALL after at least two prior lines of treatment.

All consecutive eligible patients treated during the study period were included. Exclusion criteria were: no exposure to blinatumomab, age ≥18 years at treatment initiation, diagnosis other than BCP-ALL, or insufficient medical documentation for endpoint assessment.

Because of the retrospective design and rare disease setting, no formal sample size calculation was performed.

Treatment Protocol and Administration of Blinatumomab

All patients received blinatumomab as monotherapy according to institutional treatment protocols valid at the time of therapy.

One treatment cycle consisted of a continuous intravenous infusion administered over 28 days, followed by a planned 14-day interval between cycles.

The standard dose was 15 μg/m^2/day.

Patients receiving blinatumomab as an alternative to chemotherapy generally received three cycles. Patients receiving blinatumomab as bridging therapy before hematopoietic stem cell transplantation (HSCT) received at least one cycle, with the final number of cycles determined individually according to remission status, toxicity, and transplant scheduling.

Dose interruption or treatment modification due to reduced tolerance and/or adverse events occurred in 3 patients (23.08%). In two patients, treatment was temporarily interrupted for 5 and 8 days, respectively, while in one patient the cycle was terminated on day 22.

Premedication and cytokine release syndrome prophylaxis consisted of dexamethasone and paracetamol according to institutional standards. Clemastine was additionally used in selected patients.

Data Collection

The following variables were extracted from archived medical records: sex and age, age at diagnosis, age at blinatumomab initiation, disease episode at treatment initiation, indication for blinatumomab therapy, bone marrow blast percentage, MRD status before and after treatment, cytogenetic and molecular abnormalities, serum immunoglobulin G (IgG) levels, treatment-related adverse events, relapse after treatment, survival status at last follow-up.

All data originated exclusively from routine clinical care. No additional tests or procedures were performed for research purposes.

Before analysis, all data were anonymized.

Diagnostic Procedures

Bone marrow aspiration was routinely performed before the first cycle of blinatumomab and after each completed treatment cycle.

MRD was assessed using multiparameter flow cytometry and/or polymerase chain reaction (PCR), according to the diagnostic standards available at the time of treatment and national standards applicable at the time of treatment.

Because the study covered an eight-year period, diagnostic platforms and laboratory assays evolved over time, including MRD methodologies and genetic testing panels. This may have introduced measurement heterogeneity and potential misclassification bias. However, all assessments were performed in accredited reference laboratories using contemporaneous validated procedures and clinically accepted thresholds. Results were interpreted within the clinical context of each treatment period.

Genetic abnormalities were assessed using fluorescence in situ hybridization (FISH) and/or PCR.

Serum IgG levels were measured during treatment and follow-up when clinically indicated.

Pharmacokinetic and pharmacogenetic data were not routinely available in this retrospective dataset.

Definitions and Study Outcomes

Complete remission (CR) was defined as: <5% blasts in bone marrow, no blasts in peripheral blood, no evidence of extramedullary disease, no central nervous system involvement.

MRD negativity was defined as leukemic burden $\leq 10^{-4}$ by flow cytometry or PCR.

The primary efficacy endpoint was achievement of MRD negativity after blinatumomab treatment.

Secondary efficacy endpoints included: overall survival (OS), relapse after treatment, remission status after therapy.

The primary safety endpoint was the occurrence of treatment-related adverse events.

Adverse events were graded according to the Common Terminology Criteria for Adverse Events (CTCAE), version 6.0.

Disease episodes were classified as: Episode I – from initial diagnosis to first complete remission, Episode II – from first relapse to second complete remission, Episode III – from second relapse to third complete remission.

Follow-Up

For survival analyses, time zero was defined as the first day of blinatumomab administration.

Patients were followed from treatment initiation until death or the last documented clinical contact.

For descriptive survival reporting, 12-month and 24-month overall survival estimates were predefined landmark time points, selected for clinical interpretability and comparability with previously published pediatric ALL studies.

Statistical Analysis

All statistical analyses were performed using STATISTICA software (version 13.3; StatSoft Polska Sp. z o.o., Kraków, Poland).

Continuous variables were summarized using medians with interquartile ranges (IQR) or means with standard deviations, depending on data distribution. Categorical variables were presented as absolute numbers and percentages.

Normality of distribution was assessed using the Shapiro–Wilk test.

Comparisons between groups were performed using: Student's *t*-test, Mann–Whitney *U*-test, Pearson chi-square test, NW chi-square test.

Overall survival was estimated using the Kaplan–Meier method. Differences between survival curves were assessed using the Log rank test when applicable.

Predefined exploratory subgroup analyses were performed according to treatment setting: frontline high-risk cohort, relapsed disease cohort.

Because of the limited sample size, all inferential and subgroup analyses were considered exploratory and interpreted with caution.

Missing data were infrequent and were handled using complete-case analysis for individual endpoints. A two-sided p value <0.05 was considered statistically significant.

Ethical Considerations

The use of blinatumomab in pediatric ALL treatment was conducted within a research framework approved by the Bioethics Committee of the Medical University of Silesia (approval No. PCN/0022/KB1/90/XIV/20/21), of which the present retrospective analysis formed a component. This approval covered a multicenter/non-interventional collaborative research framework involving external investigators. The present analysis included anonymized retrospective data from the Lublin center only.

The current study used exclusively anonymized archived medical records collected during routine clinical care. No intervention, treatment modification, or additional diagnostic procedures were introduced for research purposes.

No directly identifiable personal data were available to investigators.

The study was conducted in accordance with the Declaration of Helsinki and applicable national regulations.

Written institutional consent procedures covered the use of anonymized clinical data for scientific purposes. Consent had been obtained from parents or legal guardians, and from patients aged >16 years when applicable, according to local institutional policy.

Results

Patient Characteristics

The study group consisted of 13 Caucasian patients (N = 13), including 8 girls (61.54%) and 5 boys (38.46%). The median age at diagnosis was 6 years and 5 months (IQR: 5–9 years and 9 months). The median age at initiation of blinatumomab therapy was 9 years and 2 months (IQR: 6 years and 10 months-11 years and 11 months).

All 13 patients (100%) were diagnosed with B-cell precursor acute lymphoblastic leukemia (B-ALL) and were classified as high-risk. In 7 patients (53.85%), blinatumomab was administered as an alternative to conventional chemotherapy, while 6 patients (46.15%) received blinatumomab as bridging therapy prior to hematopoietic stem cell transplantation (HSCT). At the initiation of blinatumomab treatment, 7 patients (53.85%) were in episode I, 4 patients (30.77%) in episode II, and 2 patients (15.38%) in episode III. The median time between first-line treatment and initiation of blinatumomab was 7 months (IQR: 4 months-1 year and 9 months).

Genetic abnormalities were detected in 7 patients (53.85%). The KMT2A-AFF1 rearrangement was identified in 2 patients, IKZF1 mutations in 3 patients, JAK/STAT pathway mutations in 1 patient, and ETV6-RUNX1 fusion in 1 patient. Trisomy 21 was present in 2 patients. No clinically relevant genetic abnormalities were identified in 6 patients.

The median percentage of bone marrow blasts at diagnosis was 86.20% (IQR: 65.30–89.20%). At the start of blinatumomab therapy, all patients had <5% bone marrow blasts (median 1.4%, IQR: 0.4–2.6%).

Extramedullary disease was observed in 2 patients. In one patient, central nervous system (CNS) involvement marked the onset of episode II. In another patient, extramedullary disease occurred during episode I, but was not present at first relapse. Consequently, at the time of blinatumomab treatment, only one patient had active extramedullary disease.

Disease relapse after blinatumomab therapy occurred in 2 patients (15.38%), both of whom received blinatumomab as bridging therapy before HSCT, in 6 and 12 months after treatment.

The median follow-up time, defined as the period from initiation of blinatumomab therapy to death or last follow-up, was 27 months (IQR: 18–43 months).

A total of 4 deaths (30.77%) were recorded, including 2 due to disease progression and 2 due to treatment-related complications.

Detailed demographic and clinical characteristics of the patients are presented in Table 1.

Table 1 Patient Characteristics Prior to Initiation of Blinatumomab Therapy

Characteristic	Value
Sex, n(%)	
Female	8 (61.54)
Male	5 (38.46)
Age at diagnosis, years	
Median (IQR)	6.5 (5.0–9.8)
Age at diagnosis, n (%)	
<1 year	2 (15.38)
1–5 years	3 (23.08)
6–10 years	5 (38.46)
>10 years	3 (23.08)
Age at initiation of blinatumomab, years	
Median (IQR)	9.2 (6.8–11.9)
Genetic abnormalities present, n (%)	
None	6 (46.15)
IKZF1 alterations	3 (23.08)
KMT2A rearrangements	2 (15.38)
ETV6–RUNX1 fusion	1 (7.69)
Trisomy 21	2 (15.38)
Bone marrow blasts at diagnosis, %	
Median (IQR)	86.2 (65.3–89.2)
Bone marrow blasts before blinatumomab, %	
Median (IQR)	1.4 (0.4–2.6)
Disease episode at blinatumomab initiation, n (%)	
I	7 (53.85)
II	4 (30.77)
III	2 (15.38)
Indication for blinatumomab therapy, n (%)	
Treatment	7 (53.85)
Bridging therapy prior to HSCT	6 (46.15)

Abbreviations: N, number, HSCT, hematopoietic stem cells transplantation; IQR, interquartile range.

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Safety Profile

In our cohort, adverse events occurred in 9 out of 13 patients (69.23%). Grade 3 adverse events were observed in 3 of 13 patients (23.08%). No life-threatening adverse events were reported.

During blinatumomab treatment, infection-related symptoms occurred in 5 of 13 patients (38.46%), including grade 3 infections in 2 patients (15.38%). Specific infections included respiratory syncytial virus (RSV) in 3 patients (23.08%), SARS-CoV-2 in 1 patient (7.69%), and atypical Pneumocystis jirovecii infection in 1 patient (7.69%).

Neurological events were observed in 38.46% of patients. Components of immune effector cell–associated neurotoxicity syndrome occurred in 3 of 13 patients (23.08%), including limb tremors (2/13, 15.38%), altered consciousness (2/13, 15.38%), speech disturbances including aphasia (2/13, 15.38%), limb paresis (1/13, 7.69%), balance and coordination disorders (1/13, 7.69%), and headaches (1/13, 7.69%). Additionally, levetiracetam was administered prophylactically in 3 of 13 patients (23.08%) due to elevated risk and/or prior seizure episodes.

Cardiac adverse events during blinatumomab therapy included tachycardia (1/13, 7.69%), hypertension (1/13, 7.69%), minor intraventricular conduction disturbances (2/13, 15.38%), arrhythmia (2/13, 15.38%), intermittent bradycardia (1/13, 7.69%), and first-degree atrioventricular block (1/13, 7.69%). These findings were detected during routine inpatient clinical monitoring and serial electrocardiographic assessments. No patient required permanent treatment discontinuation or intensive cardiac intervention. A direct causal relationship with blinatumomab could not be established.

In our patient cohort, reduced immunoglobulin levels were observed in 2 out of 13 patients (15.38%). In both cases, this occurred after a single cycle of treatment.

Other adverse events included proctitis in 1 patient (7.69%) and pruritus in 1 patient (7.69%).

The frequency of adverse events by category, expressed as the number of patients affected in each group, is illustrated in the figure below (Figure 1).

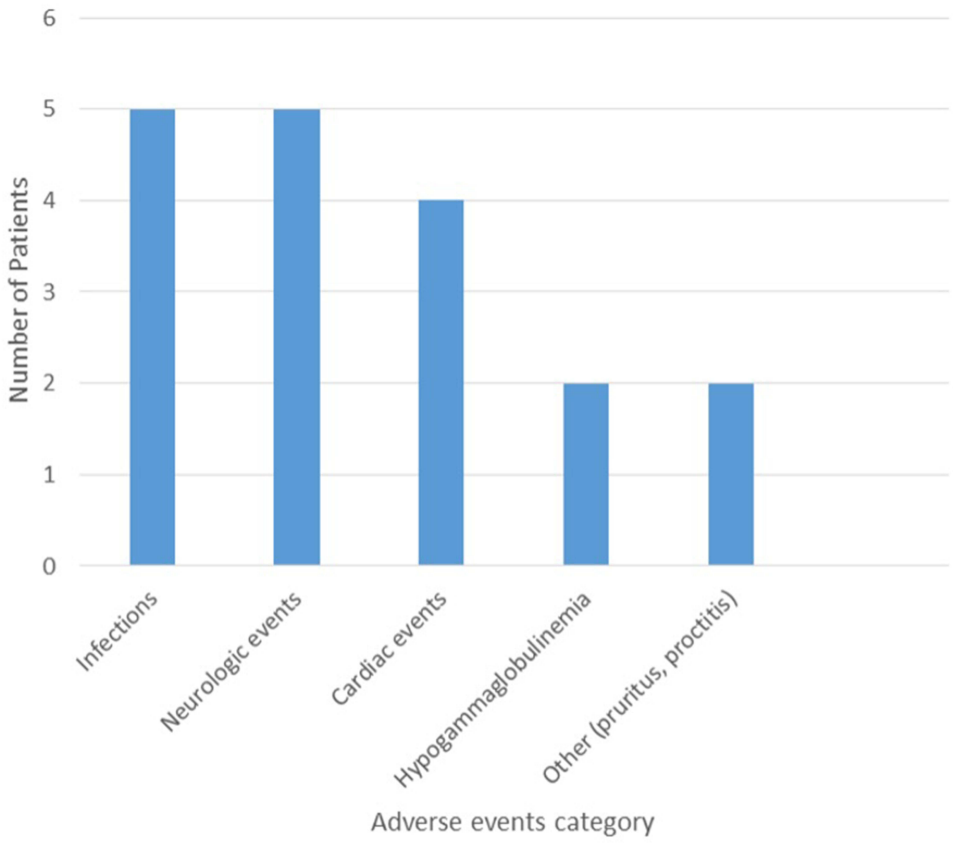

Figure 1 Distribution of adverse events by category.

Treatment Outcomes

Before starting blinatumomab therapy, 12 out of 13 patients (92.31%) were in complete remission (CR). One patient had not achieved CR.

Exploratory subgroup analyses were performed according to treatment indication (frontline high-risk cohort vs relapsed disease cohort). Because of the small number of patients in each subgroup, these analyses were considered descriptive.

MRD was positive in 8 of 13 patients (61.54%) prior to blinatumomab administration. Overall, MRD negativity was achieved in 6 of 8 patients (75.0%), including 5 of 8 (62.50%) after the first cycle and 1 of 8 (12.50%) after the second cycle. Among patients in their first episode of disease, 5 had positive MRD before blinatumomab. After one treatment cycle, 4 out of 5 patients (80%) in this subgroup achieved MRD negativity.

Kaplan-Meier analysis estimated overall survival was 83.3% at 12 months and 64.8% at 24 months. Median overall survival was not reached during the follow-up period. The survival curve is presented below (Figure 2).

Mortality did not differ significantly by sex (12.5% in females vs. 60.0% in males; $p = 0.6971$).

Age at diagnosis was not associated with survival (mean age: 7 years vs. 7 years 9 months; $p = 0.78$). Mutation status was not associated with MRD negativity after cycle 2 (85.7% without mutations vs. 50.0% with mutations; $p > 0.05$).

Age at diagnosis was not associated with MRD negativity after cycle 1 ($p = 0.812$) or cycle 2 ($p = 0.160$).

In this cohort, the disease episode (first vs. subsequent relapse) did not have a statistically significant effect on treatment response (MRD negativity) after the first cycle ($U = 7.5$, $Z = -0.48$, $p = 0.63–0.67$) or the second cycle ($U = 0.00$, $Z = 0.00$, $p = 1.00$).

It was found that the number of blasts prior to the initiation of blinatumomab therapy did not significantly affect the risk of adverse events ($t = -1.53$; $df = 11$; $p = 0.155$).

No significant differences were observed between patients who experienced adverse events and those who did not with respect to the number of disease episodes ($U = 10.5$; $Z = -1.08$; $p = 0.28$).

In the group of patients who achieved MRD negativity, 3 out of 10 (30%) died, whereas no deaths were reported among patients with positive MRD (0/2). MRD negativity after the first cycle did not significantly influence survival ($\chi^2 = 1.28$; $df = 1$; $p = 0.258$).

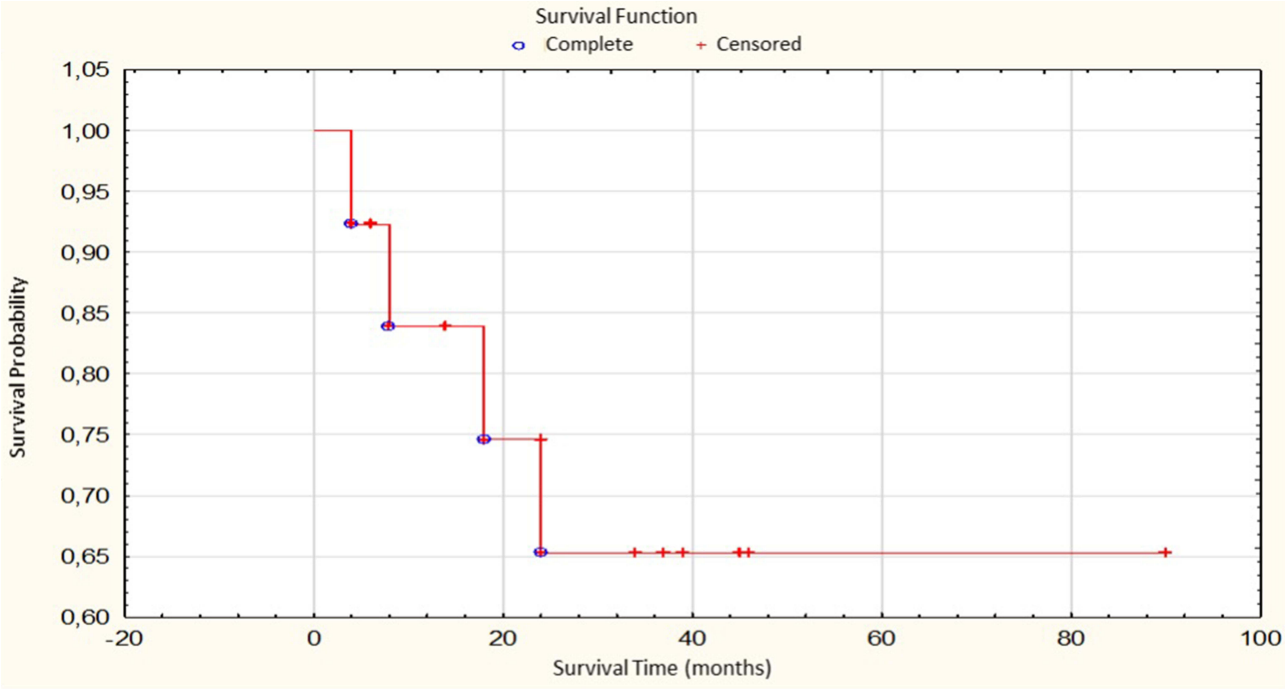

Figure 2 Kaplan-Meier estimate of the survival function for the study population.

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MRD negativity did not differ by sex after cycle 1 (87.5% vs. 75.0%; p = 0.592) or cycle 2 (100% vs. 66.7%; p = 0.101).

Time from diagnosis to blinatumomab initiation was not associated with MRD response after cycle 1 (p = 0.33) or cycle 2 (p = 1.00).

All subgroup and inferential analyses should be interpreted cautiously because of the limited sample size and low statistical power of the cohort.

Discussion

In recent years, the introduction of novel therapies, including immunotherapy and cellular therapies, has contributed to improved survival rates in patients with ALL. Blinatumomab therapy has gained clinical importance in ALL treatment, showing promising preliminary results in terms of efficacy and tolerability. However, further studies are needed to define its therapeutic value, particularly in patients with refractory or relapsed ALL, whose prognosis remains poor.

According to the available literature, the complete remission (CR) rate in patients treated with blinatumomab ranges from 38% to 59%. In the Phase I/II MT-103-205 study by von Stackelberg et al, 27 out of 70 patients (39%) achieved CR within the first two cycles.[9] In the RIALTO study, which included patients in their second or subsequent relapse, the CR rate was 59% among patients with <5% blasts at baseline (58/98).[10] In our analysis, nearly all patients were in CR prior to the initiation of blinatumomab, making it impossible to evaluate treatment efficacy using CR as an endpoint in our cohort.

Compared with CR, minimal residual disease (MRD) assessment is a more sensitive and precise measure of treatment response. In the study by Locatelli et al, MRD remission after one cycle of blinatumomab was achieved in 44 of 49 patients (90%), all of whom were in their first episode of ALL.[11] In contrast, the study by Brown et al, conducted in children and young adults in first relapse, reported an MRD negativity rate of 75% after one cycle of therapy.[12] The MRD negativity rate observed in our overall cohort was lower than those reported in the literature. However, it should be noted that our analysis included patients at different disease episodes, which was associated with a generally lower treatment response. When considering only patients in their first disease episode after one cycle, the rate of MRD negativity in our study was substantially higher, consistent with previously reported results.

For the evaluation of treatment efficacy, overall survival (OS) is an important parameter. In the MT-103-205 study, the median OS was 7.5 months (range, 4.0–11.8 months) with a median follow-up of 23.8 months. In the RIALTO study, the median OS for all patients was 13.1 months (10.2–21.3 months) with a median follow-up of 17.4 months.[9,10] A retrospective analysis by Queudeville et al reported a median OS of 11.1 months (range, 0.2–113 months) in the studied cohort, with a median follow-up of 54 months for survivors (8.9–113 months).[13] In our cohort, the median OS was not reached during the observation period; therefore, Kaplan-Meier analysis was performed. In the available studies, 12-month OS ranged from 50.8% to 55%, and 24-month OS ranged from 20.0% to 39%, whereas in our cohort, both 12- and 24-month OS were higher.[10,14] In both our analysis and the referenced studies, the patient groups consisted of individuals treated with blinatumomab who were candidates for hematopoietic stem cell transplantation (HSCT). In studies where all patients underwent HSCT, Kaplan-Meier estimated OS was substantially higher: among patients achieving complete remission, 12-month OS was 100% and 24-month OS was 85%.[15] In the study by Brown et al, 24-month OS was 71.3%, and in one retrospective analysis, three-year OS reached 85%.[12,16] These data suggest that performing HSCT after blinatumomab therapy may be associated with improved treatment outcomes in patients with high-risk ALL.

In the long-term follow-up of the RIALTO study, the median relapse-free survival (RFS) was 8.5 months (range, 4.7–14.0) with a median follow-up for RFS of 11.5 months (range, 0.0–16.3) among patients who achieved CR within the first two cycles. The median RFS for patients achieving MRD response was 8 months (3.4–10.1 months), whereas for non-responders it was 2.8 months (0.3–9.2 months).[17] In the study by von Stackelberg et al, the median RFS was 4.4 months (range, 2.3–7.6 months) with a median follow-up of 23.1 months. Patients achieving MRD-negative complete response had a longer median RFS of 7.3 months (2.7–16.4 months) compared to 1.9 months (0.8–6.0 months) in patients without MRD response.[9] In our cohort, the median RFS was not reached during the observation period.

Both chemotherapy and modern targeted therapies are associated with adverse events due to their intensity, making the evaluation of each drug's safety profile essential. In one study, grade 3 or higher adverse events during blinatumomab therapy were reported in approximately 65% of patients.[10] In Study 215, the incidence of grade ≥3 adverse events was

57.4% in the blinatumomab group compared to 82.4% in the group receiving consolidation chemotherapy.[11] In our cohort, grade 3 adverse events occurred less frequently than in these studies, and no grade 4 events were observed. These findings, along with other reports, suggest that blinatumomab may represent a safer therapeutic option compared with consolidation chemotherapy. In the study by Locatelli et al, grade 3 or higher infections occurred in 18.5% of patients treated with blinatumomab. In the same study, neurological events were reported in 48.1% of patients receiving blinatumomab, while in the RIALTO study, the rate was 42%.[11] Consistent with our results and other reports, the most frequently observed neurological adverse events include seizures and limb tremors. The incidence of infections and neurological events in our cohort aligns with observations from other centers. Cardiac adverse events, including tachycardia, conduction disturbances, and arrhythmias, were observed in 30.77% of patients. However, literature data on electrocardiographic abnormalities are limited, indicating a need for further research. Hypertension is another adverse event associated with blinatumomab, reported in 11–13% of cases.[11,18] In our cohort, the incidence was slightly lower than in these reports. Interpretation of cardiac events requires caution. Children receiving blinatumomab were hospitalized and closely monitored, including repeated electrocardiographic assessments, which may increase detection of transient or clinically minor abnormalities. In addition, prior chemotherapy exposure, electrolyte disturbances, infection, fever, anemia, and concomitant medications may also contribute to rhythm disturbances. Cardiovascular abnormalities reported during blinatumomab therapy may reflect multifactorial mechanisms, including cytokine-mediated effects, infection, electrolyte disturbances, prior cardiotoxic chemotherapy exposure, and intensive inpatient monitoring rather than direct drug toxicity alone. Recent cardio-oncology reviews of T-cell engaging therapies indicate that arrhythmias and transient conduction abnormalities may occur in the broader context of inflammatory and hemodynamic stress responses.[19] Therefore, the observed cardiac findings should not be interpreted as definitively attributable to blinatumomab. Secondary hypogammaglobulinemia is also recognized as a blinatumomab-related adverse effect. According to Locatelli et al, it occurred in 11.1% of patients receiving blinatumomab.[11] In our cohort, decreased IgG levels were observed, requiring immunoglobulin replacement therapy for periods ranging from 3 to 14 months. Long-term monitoring of this adverse effect is warranted, particularly because in adult populations treated with blinatumomab, the incidence of secondary hypogammaglobulinemia is higher than in patients receiving chemotherapy (6% vs. 0.9%). Literature data in the pediatric population are limited.[20] Among less common adverse events, authors report pruritus, constipation, abdominal pain, and rash.[11]

The interpretation of the results should take into account the limitations related to the single-center, retrospective design of the study and the small sample size. The very small sample size limits statistical power, precision of estimates, and external validity. Therefore, all subgroup and inferential analyses should be interpreted as exploratory. MRD assessment methods (flow cytometry and/or PCR) and genetic testing panels changed over the study period, which may have introduced measurement heterogeneity and potential classification bias.

Blinatumomab appears to be a potentially effective therapy for achieving MRD negativity and prolonging overall survival in patients with high-risk B-cell precursor acute lymphoblastic leukemia (HR pre-B ALL), particularly when used as bridging therapy prior to HSCT. Its use is associated with well-controlled, non–life-threatening adverse events. Future prospective studies should take into account the body's metabolic state, including normalized nutritional parameters (malnutrition and severe malnutrition), as well as pharmacokinetics and pharmacogenetics, which may influence treatment tolerance, immune system recovery, and treatment outcomes. There is also a need for prospective multicenter studies with defined response biomarkers.

Data Sharing Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to institutional and ethical restrictions.

Ethical Statement

The use of blinatumomab was approved by the Bioethics Committee of the Medical University of Silesia in Katowice (PCN/0022/KB1/90/XIV/20/21). This study is a retrospective analysis of data from the study reviewed by this committee.

Consent to Publish

Written informed consent for the scientific use and publication of anonymized clinical data was obtained from parents or legal guardians, and from patients when applicable according to local policy.

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Disclosure

The authors report there are no competing interests to declare for this work.

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