The Use of Blinatumomab in Relapsed Acute B Lymphoblastic Leukemia: Case Report

https://doi.org/10.32635/2176-9745.RBC.2025v71n4.5218EN

O Uso do Blinatumomabe na Recidiva da Leucemia Linfoblástica Aguda B: Relato de Caso

El Uso de Blinatumomab en la Leucemia Linfoblástica Aguda B Recidivante: Informe de Caso

Yhasmyn Silva Portella[1]; Everaldo Xavier dos Santos[2]; Rosa Malena Fagundes Xavier[3]

ABSTRACT

Introduction: B-type acute lymphoblastic leukemia (B-ALL), common in childhood, involves the abnormal proliferation of cells that replace normal bone marrow elements. Treatment is challenging and usually based on polychemotherapy. In relapsed cases, blinatumomab stands out as a promising therapy due to its lower cytotoxicity compared to traditional chemotherapy. This study reports the pioneering use of blinatumomab in a pediatric patient at a High Complexity Oncology Care Center in Bahia. **Case report:** A 10-year-old male patient, Jehovah's Witness, diagnosed with B-ALL, presented high-risk relapse. Due to the low response and intolerance to cytotoxic chemotherapy, immunotherapy with blinatumomab was chosen. Treatment was clinically monitored, maintaining the patient's stability, while a potential hematopoietic stem cell transplant is being planned. **Conclusion:** The study highlights blinatumomab as a promising alternative for relapsed B-ALL, emphasizing the importance of managing neurological effects and documenting clinical experiences to influence future practices.

Key words: Precursor Cell Lymphoblastic Leukemia-Lymphoma; Immunotherapy/methods; Child; Recurrence; Febrile Neutropenia.

RESUMO

Introdução: A leucemia linfoblástica aguda B (LLA-B), comum na infância, envolve a proliferação anormal de células que substituem elementos medulares normais. O tratamento é desafiador e normalmente baseado em poliquimioterapia. Em casos recidivados, o blinatumomabe se destaca como uma terapia promissora em razão da menor citotoxicidade comparada à quimioterapia tradicional. Este estudo relata o uso pioneiro do blinatumomabe em um paciente pediátrico de um Centro de Assistência de Alta Complexidade em Oncologia na Bahia. **Relato do caso:** Paciente do sexo masculino, 10 anos, Testemunha de Jeová, diagnosticado com LLA-B, apresentou recidiva de alto risco. Em virtude da baixa resposta e da intolerância à quimioterapia citotóxica, optou-se pela imunoterapia com o blinatumomabe. O tratamento foi monitorado clinicamente, mantendo-se a estabilidade do paciente, enquanto se planeja um potencial transplante de células-tronco hematopoiéticas. **Conclusão:** O estudo sublinha o blinatumomabe como promissor para LLA-B recidiva, destacando a importância de gerenciar efeitos neurológicos e documentar experiências clínicas para influenciar práticas futuras.

Palavras-chave: Leucemia-Linfoma Linfoblástico de Células Precursoras; Imunoterapia/métodos; Criança; Recidiva; Neutropenia Febril.

RESUMEN

Introducción: La leucemia linfoblástica aguda B (LLA-B), común en la infancia, implica la proliferación anormal de células que reemplazan los elementos normales de la médula. El tratamiento es un desafío y generalmente se basa en una quimioterapia con múltiples medicamentos. En los casos de recaída, blinatumomab destaca como una terapia prometedora debido a su menor citotoxicidad en comparación con la quimioterapia tradicional. Este estudio reporta el uso pionero de blinatumomab en un paciente pediátrico en un Centro de Atención Oncológica de Alta Complejidad de Bahía. **Informe del caso:** Paciente masculino de 10 años, Testigo de Jehová, diagnosticado con LLA-B, presentó recidiva de alto riesgo. Debido a la baja respuesta e intolerancia a la quimioterapia citotóxica, se optó por la inmunoterapia con blinatumomab. El tratamiento fue monitoreado clínicamente, manteniendo la estabilidad del paciente, mientras se planificaba un potencial trasplante de células madre hematopoyéticas. **Conclusión:** El estudio destaca que blinatumomab es prometedor para la LLA-B recurrente, destacando la importancia de controlar los efectos neurológicos y documentar las experiencias clínicas para influir en las prácticas futuras.

Palabras clave: Leucemia-Linfoma Linfoblástico de Células Precursoras; Inmunoterapia/métodos; Niño; Recurrencia; Neutropenia Febril.

[1]Universidade do Estado da Bahia (Uneb), Programa de Atenção em Oncologia. Salvador (BA), Brasil. E-mail: yhasmyn.portella8@gmail.com. Orcid iD: https://orcid.org/0000-0003-2614-8591.
[2]Escola de Saúde Pública da Bahia (ESPBA). Salvador (BA), Brasil. E-mail: xavierlilaz@gmail.com. Orcid iD: https://orcid.org/0009-0009-2553-3296
[3]Uneb. Salvador (BA), Brasil. E-mail: rxavier@uneb.br. Orcid iD: https://orcid.org/0000-0002-3203-8949
Corresponding author: Yhasmyn Silva Portella. Rua Waldir Pires, 328 – Centro. Lauro de Freitas (BA), Brasil. E-mail: yhasmyn.portella8@gmail.com

INTRODUCTION

Acute lymphoblastic leukemia (ALL) is a malignant neoplasm diagnosed in infancy, the most common subtype (80%) is B-cell ALL, characterized by clonal proliferation of B-lymphoid precursor cells, resulting in the replacement of adipose spaces and normal medullar elements by leukemic cells[1].

Predominantly, the diagnosis of B-ALL results from morphologic and cytochemistry analysis of neoplastic cells. The identification of specific immunophenotypic markers as CD19, CD20 and CD22, characteristic of B-lymphocytes derived-cells is crucial to differentiate B-ALL blasts from other pathologic processes[2].

Treatment of B-ALL is a significant challenge due to the strong impact on the quality of life of the patients and high cost. Its main therapeutic pillar is polychemotherapy, frequently complemented by radiotherapy and/or hematopoietic stem-cells transplantation (HSCT)[3].

Notwithstanding advances and diversity of available options, associated adverse events are frequently severe. In addition, relapses increases even more the complexity of clinical management[4]. In this context, blinatumomab is a promising therapy for relapsed B-ALL patients due to its low toxicity compared with traditional chemotherapies[5].

Its mechanism of action binds the anti-CD19 variable region in malignant B-cells to the anti-CD3 variable region in T cells. This brings in close proximity and activates T-cells which release cytotoxic substances, leading to the destruction of CD19+ tumoral cells through apoptosis and cellular lysis. After the initial elimination, blinatumomab continues to identify other malignant B-cells, keeping a continuous and effective attack[6].

In face of the potential benefits of this therapy, this report based on electronic chart information between April and July 2024 has the objective of describing and analyze the clinical and lab results, including adverse events of the first pediatric patient to take blinatumomab at a high complexity oncologic enter (Cacon) in Bahia.

The Ethics Committee of "*Universidade do Estado da Bahia (Uneb)*" approved the study, reports number 7243675 and 7298704 (CAAE (submission for ethical review) 84408624.0.0000.0057 and 84408624.0.3001.0385, respectively), in compliance with Directive 466/12 of the National Health Council (CNS)[7] for studies with human beings. The retrospective design study was based on secondary data obtained from electronic charts between April and July 2024. The informed consent form (ICF) was signed by the parent or legal guardian, but it was waived for the pediatric patient.

CASE REPORT

10-year old male patient, Jehovah's Witness, diagnosed with intermediate risk B-ALL in 2020. Treatment was initiated in the same year following the Berlin-Frankfurt-Munich (BFM) 2009[8] protocol, maintenance therapy was initiated in June 2021 and ended in 2022.

However, in August 2023, blood cell count revealed the presence of blasts and febrile neutropenia (37.8°C). The treatment was rapidly adjusted (BFM Relapse) evolving to high medullar risk. Despite the initial management, the patient did not tolerate the treatment, leading to the modification of the protocol of maintenance due to intense aplasia. Nevertheless, this change was ineffectual.

Because of the intense medullar aplasia and recurring infections, the patient did not tolerate conventional chemotherapy. It was decided to utilize blinatumomab as treatment of consolidation, in preparation for a potential HSCT. This decision followed the criteria of indication adopted by the National Health System (SUS): use in B-ALL (markers CD19, CD20, CD22); cerebrospinal fluid (CSF) without infiltration; early relapse (<10 months); 3rd (or +) consolidation phase; age range <18 years; high risk first medullar relapse diagnosed by immunophenotyping[6].

The treatment initiated in May 2024 with the patient admitted to the pediatric semi-intensive care unit (ICU) during the first nine days. IV blinatumomab was prescribed through a peripherally inserted central catheter (PICC), at a 5 mcg/m²/day dosage from D1 to D7, increasing to 15 mcg/m²/day from D8 to D28.

At D1, pre-medication included dexamethasone administered eight hours before and 30 minutes after beginning the continuous infusion of chemotherapy. At D2, the patient presented mild fever (37.9°C) and a self-limited episode of paresthesia in the hands. At D3, fever escalated to 38.1°C, treated with sodium dipyrone 1g, while the infusion with blinatumomab was kept because the vital signs were stable. In the same day, he was unable to stay erect but without dizziness or other complaints. Surveillance was intensified to monitor possible neurological complications that did not repeat in the other days of the therapy.

Renal function presented temporary creatinine elevation (0.3 mg/dL to 0.7 mg/dL), stabilizing in D4 at 0.6 mg/dL. Fever reappeared only in D9 (37.8%) without other complications. Peripheral and central blood culture were negative and fever was controlled with tazocin, vancomycin and amikacin, that were suspended in D23 after clinical stabilization. Finally, at D28, at the

end of the blinatumomab infusion, a new myelogram was collected to evaluate the therapeutic response (Table 1).

The patient tolerated well the blinatumomab infusion, presenting mild adverse events as fever, paresthesia in the hands and transitory bradycardia (up to 60 bpm) that did not require specific treatment. In addition, there was no liquid retention, oral diet was well accepted, no vomits occurred and weight gain of 2.1 kg. Febrile neutropenia episodes were treated accordingly.

Only one cycle of the medication was administered, followed by maintenance, follow-up and regular evaluations of the medulla. The transplantation team decided to continue monitoring the patient because the donor was haploidentical, presenting higher risks compared to 100% compatible donor.

DISCUSSION

To treat relapsed B-ALL in pediatric patients is challenging because from 20% to 30% of the children relapse after the first remission. Although aggressive therapy can be necessary, it brings significant risks as bone marrow failure and more susceptibility to severe infections. In these cases, especially with medullar aplasia, immunotherapy is an alternative for targeted treatments[4].

Consequently, the use of blinatumomab for relapsed B-ALL patients has been effective, especially in cases of negative minimal residual disease. A systematic review[5] concluded that the immunotherapy reflects the progress of ALL treatment causing less adverse events, better quality of life and low mortality compared to standard chemotherapy.

Because of religion constraints – Jehovah's Witness – the patient could not be transplanted, except in a life-threatening scenario and immunotherapy stood out as a promising, less aggressive strategy than cytotoxic therapy which could demand additional transfusions especially with intense medullar aplasia.

The patient's clinical conditions should guide the choice between immunotherapy and cytotoxic chemotherapy to treat early medullar relapse. Immunotherapy has the potential to reduce relapses while strengthening the immune system, enabling a long-lasting response and preparing patients for a potential HSCT.

Among recent studies investigating the use of blinatumomab as a preparation for HSCT, stands out a research which evaluated 19 children treated with the medication followed by HSCT, nine of them successfully. Remarkably, most of them (11 children) completed only one cycle of the drug. Among those submitted to HSCT with negative minimal residual disease, none relapsed, indicating that this might be a promising curative strategy[9].

The most common adverse events associated with blinatumomab are reactions to perfusion (67.2%), infections (63.0%), pyrexia (59.8%) and febrile neutropenia (28%)[6]. However, the major concern is the neurotoxicity (NT) (13.8%)[6], that can be explained by the immune activation and cytokine release, exhibiting an array of intensities since mild symptoms up to severe life-threatening complications, requiring immediate intervention[10].

In a study involving six patients with B-ALL who received blinatumomab post-HSCT, the treatment was interrupted in half of the cases due to severe toxicities, mainly grade III NT and sepsis. This scenario emphasizes the importance of a thorough monitoring during treatment[11] to ensure the early detection and effective management of neurologic adverse reactions.

Another critical issue is the update of the protocol of blinatumomab in SUS which currently covers, but one cycle of treatment[12], in addition to expanding the therapeutic guidelines to include adults, as only patients aged 18 years or less are covered at the moment. Apparently, investments in researches and broader indications and use of the medication are essential to make this initiative a reality.

CONCLUSION

This study reinforces the role of blinatumomab as a promising option for patients with relapsed B-ALL offering valuable clinical insights, especially in cases aggravated by aplasia and severe adverse events. Its

Table 1. Immunophenotyping and minimal residual disease before and after blinatumomab

Period	Treatment	Immunophenotyping Profile	MRD
August/2023	Pre-blinatumomab	20.83% of immature and aberrant B-lymphoid lineage cells	Negative
June/2024	Post-blinatumomab	0.32% of immature B lymphoid lineage cells	Negative

Caption: MRD = minimal residual disease.

therapeutic viability and the importance of documenting and sharing clinical experiences can potentially impact future practices and stimulate new studies. In addition, understand and manage neurologic adverse events, mainly in the central nervous system are pivotal to optimize the therapy and promote advances in future treatments.

ACNOWLEDGMENT

To the pharmacist Aline Miranda who facilitated the communication with the medical team, critical for the success of this study. To Dr. Ana Maria Marinho, the physician in charge of the treatment and follow-up of the patient.

CONTRIBUTIONS

Yhasmyn Silva Portella contributed to the conceptualization and design of the study, acquisition, analysis and interpretation of the data, writing and critical review. Rosa Malena Fagundes Xavier and Everaldo Xavier dos Santos contributed to the writing and critical review. All the authors approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

DATA AVAILABILITY STATEMENT

All content underlying the text is contained in the manuscript.

FUNDING SOURCES

None.

REFERENCES

1. Gurbuxani S, Wynne JP, Larson RA. Acute lymphoblastic leukemia: clinical presentation, diagnosis, and classification. In: Eaderl SH, Kantarijian HM, Estey E. Hematologic Malignancies. Cham: Springer; 2020. p. 157-67. doi: 10.1007/978-3-030-53633-6_10
2. Farias MG, Castro, SM. Diagnótico laboratorial das leucemias agudas. J Bras Patol Med Lab. 2004;40(2):91-8. doi: https://doi.org/10.1590/S1676-24442004000200008
3. Pedrosa F, Lins M. Leucemia linfóide aguda: uma doença curável. Rev Bras Saude Mater Infant. 2022;2(1):63-8. doi: https://doi.org/10.1590/S1519-38292002000100010
4. Souza C, Viana MB, Oliveira BM. Recidiva da leucemia linfoblástica na criança: experiência do Serviço de Hematologia do Hospital das Clínicas da UFMG (1988-2005). RMMG. 2008;18(4Supl1);S55-S62. [Acesso 2025 mar 7]. Disponível em: https://rmmg.org/artigo/detalhes/1401
5. Gonçalves RN, Nascimento A, Chança RD, et al. Eficácia e segurança do blinatumomabe no tratamento da leucemia linfoblástica aguda: revisão sistemática da literatura. Rev Bras Cancerol. 2024:70(1);e-124482. doi: https://doi.org/10.32635/2176-9745.RBC.2024v70n1.4482
6. Ministério da Saúde (BR), Secretaria de Ciência, Tecnologia, Inovação e Insumos Estratégicos em Saúde. Protocolo de uso do Blinatumomabe para Leucemia Linfoblástica Aguda (LLA) B derivada pediátrica em primeira recidiva medular de alto risco. Brasília, DF: Comissão Nacional de Incorporação de Tecnologias no Sistema Único de Saúde; 2022 (acesso em 2024 ago 4). p. 38. Disponível em: https://www.gov.br/conitec/pt-br/midias/consultas/relatorios/2022/20221206_relatorio-pu-blinatumomabe_cp_90.pdf
7. Conselho Nacional de Saúde (BR). Resolução n° 466, de 12 de dezembro de 2012. Aprova as diretrizes e normas regulamentadoras de pesquisas envolvendo seres humanos [Internet]. Diário Oficial da União, Brasília, DF. 2013 jun 13 [acesso 2025 abr 17]; Seção 1:59. Disponível em: https://bvsms.saude.gov.br/bvs/saudelegis/cns/2013/res0466_12_12_2012.html
8. Laks D, Longhi F, Wagner MB, et al. Avaliação da sobrevida de crianças com leucemia linfocítica aguda tratadas com o protocolo Berlim-Frankfurt-Munique. J. Pediatr. 2023;79(2):149-58. doi: https://doi.org/10.1590/S0021-75572003000200010
9. Zamperlini G, Gouveia RV, Ginani VC, et al. Resultado do transplante de células-tronco hematopoiéticas com doares alternativos após blinatumomab em crianças com leucemia linfóide aguda de linhagem B (LLA-B) recidivada ou refratária. Hematol Transfus Cell Ther. 2021;43(S1):S176-7. doi: https://doi.org/10.1016/j.htct.2021.10.300
10. Pinto EV, Costa IK, Pereira OUM, et al. Neurotoxicidade relacionada ao uso de blinatumomabe: um estudo descritivo de relato de caso. Hematol Transfus Cell Ther. 2023;45(S4):S309. doi: https://doi.org/10.1016/j.htct.2023.09.606
11. Puls ML, Silva RL, Fernandes PA, et al. Blinatumimab na leucemia linfoide aguda-B em contexto de pós-transplante de células tronco hematopoiéticas: experiência de dois serviços de referência. Hematol Transfus Cell Ther. 2022;44(S2):S193-4. doi https://doi.org/10.1016/j.htct.2022.09.326

12. Ministério da Saúde (BR), Gabinete do Ministro. Portaria GM/MS nº 2.251, de 8 de dezembro de 2023. Inclui, na Tabela de Procedimento, Medicamentos, Órteses, Próteses e Materiais Especiais do SUS os procedimentos para tratamento da Leucemia Linfoblástica Aguda (LLA) B derivada pediátrica em primeira recidiva medular de alto risco [Internet]. Diário Oficial da União, Brasília, DF.: 2023 dez 11 [acesso 2025 jan 15]; Seção 1, 234. Disponível em: https://www.in.gov.br/web/dou/-/portaria-gm/ms-n-2.251-de-8-de-dezembro-de-2023-529555034

Recebido em 8/4/2025
Aprovado em 15/7/2025

Scientific-Editor: Anke Bergmann. Orcid iD: https://orcid.org/0000-0002-1972-8777