Optimizing Blinatumomab Access for Low- and Middle-Income Countries: Feasibility of a Shortened, Vial-Sharing, Outpatient Approach for Pediatric ALL

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DOI https://doi.org/10.1200/GO-25-00469

ABSTRACT

PURPOSE This study aims to evaluate the safety, feasibility, effectiveness, and cost-saving potential of a shortened, vial-sharing outpatient blinatumomab regimen for treating relapsed or refractory (R/R) ALL in children.

MATERIALS AND METHODS We conducted a retrospective study of pediatric patients with R/R B-cell ALL (B-ALL) treated with a shortened outpatient blinatumomab regimen (<21 days), aiming to achieve a negative measurable residual disease (MRD) remission before hematopoietic stem-cell transplantation (HSCT).

RESULTS Twelve patients were included: three (25%) with primary refractory disease and nine (75%) with relapse. The median follow-up time was 33 months (range, 10-76 months). Blinatumomab was administered for a median of 19 days (range, 11-21), with 75% (9 of 12) of patients completing treatment entirely on an outpatient basis. Five patients (62%) achieved CR with undetectable MRD, and all four patients who initiated treatment because of persistent MRD achieved MRD clearance (100%). Ten patients (83%) proceeded to haploidentical HSCT. The estimated 3-year overall survival (OS) was 54%, and the relapse-free survival (RFS) was 44%. These optimization measures resulted in a 43% reduction in drug-related expenditures.

CONCLUSION Reduced-duration outpatient blinatumomab shows promise as a context-adapted strategy for heavily pretreated pediatric patients with ALL. Given the small retrospective cohort, these findings should be interpreted with caution.

ACCOMPANYING CONTENT

Protocol

Accepted December 23, 2025
Published February 20, 2026

JCO Global Oncol 12:e2500469

INTRODUCTION

ALL is the most common cancer in childhood. In Mexico, the estimated incidence is 79 new cases per million children younger than 18 years.[1] While survival rates in high-income countries (HICs) exceed 90%, the overall survival (OS) in Mexico remains around 60%,[2] a disparity driven by delayed diagnosis, limited access to timely and adequate treatment, treatment abandonment, and unequal distribution of health care resources.[3,4]

Relapsed or refractory ALL (R/R ALL) occurs in approximately 10%-15% of children undergoing treatment.[5] The prognosis in this group is influenced by factors such as site and timing of relapse, with conventional chemotherapy achieving a 5-year OS of only 35%.[6] Further intensification of chemotherapy has not improved outcomes because of increased toxicity,[7] and therefore, improving access to immunotherapies, supportive care, and hematopoietic stem-cell transplantation (HSCT) is essential, especially in resource-limited settings.[3]

Blinatumomab, a bispecific T-cell engager targeting CD19, has emerged as an effective therapy for patients with R/R B-ALL, facilitating measurable residual disease (MRD) clearance and serving as a bridge to HSCT.[8-10] Standard treatment consists of a continuous 28-day intravenous infusion. Clinical trials (identifiers: NCT02393859, NCT02101853) have demonstrated its efficacy and tolerability, establishing it as the standard of care in this setting.[9-11] A recent cost-effectiveness analysis in Mexico found that blinatumomab offers a significant survival benefit in children with high-risk first-relapsed B-cell ALL, yielding an additional 5.11 life-years at an incremental cost-effectiveness ratio of MXN 121,526 per life-year gained. This suggests that blinatumomab is highly cost-effective based on the Mexican willingness-to-pay threshold.[12]

CONTEXT

Key Objective

To evaluate the feasibility, safety, and cost-effectiveness of shortened, vial-sharing outpatient blinatumomab regimens for pediatric patients with relapsed or refractory B-cell ALL (R/R B-ALL) in low- and middle-income countries, aiming to expand access to immunotherapy in resource-limited settings.

Knowledge Generated

The adapted blinatumomab regimen achieved a 62.5% complete remission rate and 100% measurable residual disease clearance, with low toxicity and no severe adverse events. Implementation of vial-sharing and shortened infusion strategies reduced drug-related costs by 43%, demonstrating a practical and sustainable approach to optimize treatment access.

Relevance

Although limited by the small, retrospective cohort, these findings provide preliminary evidence that context-adapted immunotherapy is both feasible and safe in resource-constrained environments, supporting its broader evaluation through multicenter prospective studies.

Despite the growing evidence supporting the use of blinatumomab, its implementation in low- and middle-income countries (LMICs) remains challenging. Financial and logistical barriers, including its high cost and the infrastructure required for continuous 28-day intravenous infusion, limit access to the full treatment cycle for many patients in public health care systems. Strategies such as dose reduction, outpatient administration, and shortened infusion duration may improve treatment feasibility and sustainability.[13,14]

Prolonged exposure to CD19xCD3 bispecific like blinatumomab may lead to T-cell exhaustion and reduced cytotoxicity over time. In vitro studies with AMG 562 have shown that exhaustion markers increase with continuous stimulation, whereas treatment-free intervals can help restore T-cell function. These findings support the rationale for shorter or intermittent dosing to preserve efficacy.[15]

Emerging evidence suggests that shorter blinatumomab regimens may still be effective, particularly in patients with low disease burden.[16,17] Nevertheless, the long-term impact of abbreviated courses on survival outcomes remains to be fully elucidated.

At our transplant center, where most patients are uninsured and public financial support is limited, full blinatumomab regimens are often unaffordable. In response, we implemented an affordability-adapted protocol involving a single, shortened, vial-sharing outpatient cycle of blinatumomab in children with R/R B-ALL who had failed at least two reinduction regimens and were HSCT candidates.

The primary objective of this study was to evaluate the feasibility and effectiveness of the vial-sharing and shortened outpatient blinatumomab regimen in achieving complete remission with MRD negativity before HSCT. We also aim to assess its toxicity, cost-saving, and impact on 3-year OS and relapse-free survival (RFS).

MATERIALS AND METHODS

Study Design

This retrospective single-center study included pediatric patients with R/R B-ALL treated between 2020 and 2024 at Hospital Universitario "Dr José Eleuterio González." Patients who were unable to afford or complete the conventional 28-day blinatumomab regimen received a shortened, outpatient course under compassionate-use approval, with the goal of proceeding to HSCT.

Eligible patients were 0-16 years old, had undergone at least two previous reinduction regimens, and presented with fewer than 5% bone marrow blasts but persistent MRD positivity. All had a suitable donor and completed pretransplant evaluations. Inclusion also required residence within 1 hour of the hospital and caregiver capability for outpatient management, including pump handling and early recognition of adverse events. Exclusion criteria comprised active extramedullary disease, uncontrolled infection, major organ dysfunction, or the absence of a feasible HSCT plan. The study protocol was reviewed and approved by the Institutional Ethics and Research Committee.

Treatment Protocol

All patients received a shortened, outpatient blinatumomab regimen designed to optimize vial utilization and reduce hospitalization costs. Therapy was delivered as a single cycle of continuous infusion over ≤21 days (range, 7-21) using a Q-Core Sapphire portable pump (Amgen Inc, Thousand Oaks, CA). Blinatumomab was initiated at as a continuous 24-hour infusion at 5 $\mu g/m^2/d$ for 4-7 days, followed by

15 μg/m²/d as a continuous 24-hour infusion for 10-14 days; patients with breakpoint cluster region–Abelson fusion gene positive ALL received concurrent dasatinib (60 mg/m²/d, divided twice daily). Standard premedication with dexamethasone (6 mg/m², single dose) was administered before infusion initiation and dose escalation. Written informed consent was obtained from the parents or legal guardians of all participants.

Caregivers participated in a one-hour structured session covering adverse effect recognition (early signs of cytokine release syndrome [CRS]), including the use of a written monitoring checklist for home observation and pump handling. Written materials and 24/7 telephone access to the medical team were provided. Toxicities were graded per Common Terminology Criteria for Adverse Events v5.0 and managed with supportive measures or corticosteroids as indicated.

Patients achieving MRD-negative complete response proceeded to HSCT using either matched related or haploidentical donors, conditioned with cyclophosphamide, fludarabine, and melphalan with or without total body irradiation, followed by post-transplant cyclophosphamide, cyclosporine, and mycophenolate for graft-versus-host disease prophylaxis. Further procedural details are summarized in Table 1.

TABLE 1. Short-Course Blinatumomab Regimen, Supportive Measures, and Transplantation Protocol

Component	Description
Blinatumomab regimen	Short-course regimen defined as a single cycle administered over ≤21 days (range, 7-21), delivered in the outpatient setting via continuous infusion using a Q-Core Sapphire portable pump (AMGEN)
Dosing	Initiated as a continuos 24-hours infusion at 5 μg/m²/d for 4-7 days, followed by 15 μg/m²/d for 10-14 days. Patients with *BCR-ABL*–positive ALL received concurrent dasatinib 60 mg/m²/d, divided twice daily
Premedication	Dexamethasone 6 mg/m², single dose administered before infusion initiation and after dose escalation to prevent CRS
Caregiver training	One-hour structured session on adverse effect recognition (early CRS signs), home monitoring, and pump handling. Families received a written checklist and 24/7 phone access to the medical team
Toxicity grading	Adverse events graded per CTCAE version 5.0
Toxicity management	Supportive care with hydration, antipyretics, and close monitoring. For moderate/severe CRS or neurotoxicity, blinatumomab infusion was paused, dexamethasone 10 mg/m²/d, divided every 12 hours was administered, and tocilizumab was reserved for refractory cases. Hospital admission occurred when clinically indicated
Optimization strategies for vial utilization	(1) Vial sharing with stability-guided storage: Vials reconstituted and fractionated under sterile conditions and stored at 2°C-8°C per institutional policy (2) Synchronized compounding: Multiple patient doses prepared simultaneously to minimize waste (3) Infusion-time extension: Remaining trace volumes (<0.5 mL) infused over 2-8 additional hours for the final patient
Transplant indication	Patients achieving CR with MRD negativity proceeded to HSCT once feasible. Matched related or haploidentical donors were used when unrelated donors were unavailable
Conditioning regimen	Cyclophosphamide 350 mg/m²/d once daily and fludarabine 25 mg/m²/day IV once daily (days −5 to −3); melphalan 140-210 mg/m²/d IV once daily (day −2); with or without total body irradiation (2 Gy). Infusion performed on day 0
GVHD prophylaxis	Cyclophosphamide 50 mg/kg/d IV once daily (days +3 and +4); oral cyclosporine and mycophenolate mofetil starting on day +5

Abbreviations: *BCR-ABL*, breakpoint cluster region–Abelson; CR, complete response; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; GVHD, graft-versus-host disease; HSCT, hematopoietic stem-cell transplantation; MRD, measurable residual disease.

Optimization Strategies for Vial Utilization

To maximize drug yield from each vial and curb avoidable waste, we adopted three complementary interventions:

1. Vial sharing with stability-guided storage: Each blinatumomab vial was reconstituted with a validated stabilizing solution and divided into the maximum possible number of infusion bags under a certified laminar-flow hood. Prepared bags were labeled and refrigerated (2°C-8°C) for the duration supported by stability data and institutional policy, ensuring sterility and potency throughout the allotted in-use period.
2. Synchronized compounding for multiple patients: When two or more patients were scheduled to receive blinatumomab on the same day, all doses were prepared in a single session. This simultaneous fractionation allowed residual volumes from one dose to be transferred directly to the next, under a certified laminar flow hood. This approach ensured sterile handling, reduced individual vial wastage, and improved workflow efficiency.
3. Infusion time extension for trace volumes: If a minimal amount of drug (<0.5 mL) remained after compounding, the infusion for the final patient was prolonged by 2-8 additional hours.

Response and Outcome Definitions

Since all patients had a low leukemic burden at baseline (<5% blasts), treatment response was evaluated according to MRD kinetics. Complete response (CR) was defined as MRD negativity by flow cytometry, with hematologic recovery (absolute neutrophil count ≥1 × 10⁹/L and platelets ≥100 × 10⁹/L). Partial response (PR) indicated a ≥1-log reduction in MRD with residual detectable disease and hematologic recovery. Stable disease referred to unchanged MRD levels,

whereas progressive disease was defined by increasing MRD, ≥5% marrow blasts, >25% circulating blasts, or new extramedullary involvement. MRD clearance referred to conversion from detectable MRD (≥0.01%) to undetectable levels.

MRD was assessed by standardized EuroFlow eight-color flow cytometry on a FACSCanto II cytometer (BD Biosciences, San José, CA), with negativity defined as <0.01% and a lower detection limit of 10^{-6}. Data were analyzed using Infinicyt software (Cytognos SL, Polígono La Serna, Salamanca, Spain).

OS was measured from the start of blinatumomab to death or last follow-up, and RFS from the same date to relapse or death, whichever occurred first. Relapse was defined as ≥5% marrow blasts or extramedullary recurrence after previous remission.

Statistical and Cost Analyses

A descriptive analysis was performed. Quantitative variables were summarized as medians with ranges, and categorical variables as absolute frequencies and percentages. OS and RFS were calculated from Day 1 of the first blinatumomab infusion to the date of death, last follow-up, or documented relapse. Patients who were alive and progression-free at the time of analysis were censored at their last known follow-up. Survival probabilities were estimated using the Kaplan-Meier method.

A descriptive cost analysis was also conducted, focusing exclusively on drug-related expenditures. For each patient, the actual number of blinatumomab vials used under the implemented vial-optimization strategies and the corresponding real costs were recorded. To estimate the theoretical cost without these measures, the total number of vials required for a conventional 28-day regimen was calculated, assuming no vial sharing and the disposal of residual volumes. Each vial of blinatumomab was priced at 35,000 Mexican pesos ($1,902 US dollars [USD]), using an exchange rate of $1 USD = 18.4 MXN to standardize comparisons. Hospital-related costs associated with medical care, infusion equipment, and supportive care were not included in the analysis.

RESULTS

Patient and Disease Characteristics

Between 2020 and 2024, 19 pediatric patients with R/R B-ALL were evaluated for blinatumomab therapy at Hospital Universitario "Dr José Eleuterio González."

Three patients (15.7%) who could afford the conventional 28-day regimen were excluded as they received standard duration treatment. In addition, patients were excluded because of the presence of extramedullary disease (n = 2), bone marrow blasts >5% (n = 1), or the absence of an eligible hematopoietic stem-cell donor (n = 1).

The implementation of vial optimization and shortened-infusion strategies enabled 12 patients meeting inclusion criteria to initiate treatment.

Among these 12 patients, three (25%) had primary refractory disease and nine (75%) presented with relapse, with a median time to relapse of 10.5 months (range, 5-29) from initial diagnosis. The median follow-up was 33 months (range, 10-76). At diagnosis, nine patients (75%) were classified as high-risk, two (16.7%) as intermediate-risk, and one (8.3%) as standard-risk (Table 2).

In five patients (41%), molecular panel testing was not available. Among the remaining patients, two (16.5%) harbored the *KMT2A–AF1q* fusion gene [t(4;11)(q21;q23)],

TABLE 2. Baseline Characteristics, Disease Status, and Cost Comparison With the Blinatumomab Short-Course Optimized Vial-Sharing Strategy

Characteristic	Patients, No. (%)
Sex	
Male	8 (66)
Female	4 (33)
Age, median (range)	4.5 years (7 months to 15 years)
Risk at diagnosis	
High	9 (75)
Intermediate	2 (16.5)
Low	1 (8.5)
Fusion gene	
KMLT2a-AFI1, t(4;11)(q21;q23)	2 (16.5)
ETV6-RUNX1, t(12,21)(p13;q22)	2 (16.5)
BCR-ABL (m-bcr, P190) t(15,17)	1 (8.5)
None	2 (16.5)
None available	5 (41)
Disease status at blinatumomab initiation	
1st relapse	7 (58)
2nd relapse	2 (16.5)
Refractory	3 (25)
Disease status at blinatumomab initiation	
1%-5%	8 (66.6)
Measurable residual disease–positive	4 (33.3)
Vials	
Vials used, median (range)	5.5 (3-16)
Vial used, standard 28 days (range)	9 (7-25)
Cost, USD	
Total cost for the optimized vial-sharing short-course strategy	$142,643
Total cost for the standard 28-day regimen	$251,086

Abbreviaitions: BCR-ABL, breakpoint cluster region–Abelson; USD, US dollars.

two (16.5%) carried the *ETV6–RUNX1* fusion [t(12;21)(p13;q22)], and one (8.5%) presented the *BCR–ABL* fusion, whereas two patients (16.5%) had no detectable fusion gene.

Three cases of infant leukemia were included. In two of them, molecular panel testing was not available; however, they were classified as high risk because of presenting with hyperleukocytosis (>300,000/μL) at diagnosis and refractory disease after induction. The patient with available molecular testing showed the *KMT2A–AF1q* fusion [t(4;11)(q21;q23)] and also presented with hyperleukocytosis at diagnosis.

All patients had received intensive reinduction chemotherapy before blinatumomab, with a median of three previous treatment lines (range, 2-5). At blinatumomab initiation, eight patients (67%) had persistent disease >1%, whereas four (33%) were in morphological remision but remained MRD-positive (Table 3).

Treatment and Toxicity

The median duration of blinatumomab administration was 20 days (range, 11-21), with a median of 5.5 vials used per patient (range, 3-16). Four patients experienced treatment delays exceeding 7 days, primarily because of venous access challenges or logistical limitations related to frequent hospital visits. Overall, nine patients (75%) completed the entire course in the outpatient setting.

CRS occurred in four patients (33%). One case of grade 1 CRS was managed entirely in the outpatient setting with antihistamines, hydration, and antipyretics. Three patients required short hospitalizations—two with grade 1 CRS (fever and rash) and one with grade 2 CRS (hypotension). The median duration of hospitalization was 3 days (range, 2-6). All were successfully managed with intravenous hydration and dexamethasone (10 mg/m²/d, divided every 12 hours). In the patient who developed hypotension, blinatumomab infusion was temporarily interrupted for 5 hours and then safely resumed. No patient required tocilizumab.

No transfusion support was needed during treatment. Three patients developed moderate neutropenia; notably, no episodes of febrile neutropenia or catheter-related infections were observed.

Cost Analysis

The median number of vials used per patient with these strategies was 5.5 (range, 3-16), whereas the estimated number required for a conventional 28-day regimen without optimization would have been 9 (range, 7-25).

Through the implementation of a shortened infusion schedule combined with vial-sharing and dose-optimization strategies, treatment for all 12 patients was completed using a total of 75 vials of blinatumomab, corresponding to an actual cost of $142,663 USD. Based on cost projections, a conventional 28-day regimen would have required approximately 132 vials, with an estimated total cost of $251,086 USD. Overall, these optimization measures resulted in the use of 57 fewer vials and a 43% reduction in drug-related expenditures.

Clinical Outcomes

Of the 12 patients included, five (42%) achieved complete response (CR) with undetectable MRD, four (33%) achieved MRD clearance, one (8%) had a PR, and two (16%) experienced disease progression. Overall, nine patients (75%) proceeded to HSCT (Table 4).

Among the eight patients with a disease burden >1%, five (62%) achieved CR with MRD negativity and underwent HSCT. Of these, three remain alive in remission, whereas two died—one because of relapse at day +380 post-transplant and another because of infectious complications at day +116 while in remission. Two patients (25%) developed rapid disease progression with circulating blasts, leading to early discontinuation of therapy (on days 11 and 13). One patient (12%) achieved a partial MRD response, with a reduction in disease burden from 1.7% to 0.06%. Among those who did not achieve a complete response, two patients died and one remains under palliative care.

All four patients who initiated blinatumomab with <1% blasts achieved MRD negativity and subsequently underwent HSCT. Three (75%) remain alive and in remission, whereas one died on day +41 post-transplant because of thromboembolic complications.

At a median follow-up of 33 months (10-76), the estimated 3-year OS was 54% and the RFS was 44% (Fig 1). Notably, the 3-year RFS among transplanted patients was 54%, compared with 0% in nontransplanted patients (P = .001).

DISCUSSION

In LMICs such as Mexico, access to targeted therapies remains constrained by economic, infrastructural, and policy-related health care barriers. Strict adherence to treatment protocols developed in HICs is often unfeasible, underscoring the need for pragmatic adaptations to improve accessibility. Modifying drug dose, duration, or administration schedules represents a viable, evidence-informed approach to promoting greater equity in cancer care.[13]

At our institution, the implementation of a shortened, vial-sharing, outpatient-based blinatumomab regimen markedly improved access to immunotherapy for children with R/R B-ALL. This approach enabled 75% of patients who had failed intensive chemotherapy to proceed to HSCT, with 3-year OS and RFS rates of 54% and 44%, respectively, which are favorable outcomes within this high-risk population. All patients had received two or more previous intensive

TABLE 3. Patient Characteristics, Treatment Response, and Outcomes of Pediatric Patients Receiving Short-Course Blinatumomab

Age/Sex	Preblinatumomab Therapy	Disease Status at Blinatumomab Initiation	Course Duration (days)	Outpatient/ Toxicity	Response to Blinatumomab	Postblinatumomab Therapy	Current Status
7 months/ M	3 lines of Interfant-06 TACL-Bz (2)	4.4% refractory	20 days	No/Yes, fever	CR × MRD	Haplo-HSCT	Dead because of post-HSCT relapse (+380)
12 years/ M	3 lines of total XV IDA-FLAG TACL-Bz	4.18% refractory	19 days	Yes/No	CR × MRD	Haplo-HSCT	Alive in remission
11 months/ M	2 lines of Interfant-06 TACL-Bz	3.2% very early 1st relapse	20 days	Yes/neutropenia	CR × MRD	Haplo-HSCT	Alive in remission
5 years/F	2 lines of BFM IDA-FLAG TACL-Bz	2.5% 2nd relapse	15 days	Yes/No	CR × MRD	Haplo-HSCT	Dead because of pneumonia on day +116 of HSCT
9 months/ M	3 lines of Interfant-06 BFM high-risk Blocks TACL-Bz	4.5% 1st relapse/refractory	13 days	Yes/neutropenia	PD (blast cells in peripheral blood)	Palliative care	Dead
4 years/F	3 lines of total XV UKALL3 TACL-Bz	3.65% 1st relapse	11 days	Yes/No	PD (blast cells in peripheral blood)	Palliative care	Alive in relapse
15 years/ M	2 lines of total XV UKALL3 + imatinib	1.8% refractory	20 days	No/Yes, fever, hypotension	CR × MRD	Haplo-HSCT	Alive in remission
7 years/M	3 lines of BFM, TACL-Bz, Capizzi	1.6% 2nd relapse	19 days	Yes/No	PR 0.06%	TACL-Bz Haplo-HSCT	Dead because of sepsis on day +15 of HSCT
3a/F	2 lines of BFM90 TACL-Bz	0.14% 1st relapse	21 days	No/Yes, rash, neutropenia	MRD clearance	Haplo-HSCT	Dead because of thrombosis on day +41 of HSCT
2a/M	2 lines of BFM90 TACL-Bz	0.13% 1st relapse	21 days	Yes/No	MRD clearance	Haplo-HSCT	Alive in remission
6a/F	4 lines of total XV BFM high-risk blocks IDA-FLAG TACL-Bz	0.06% 1st relapse	20 days	Yes/rash	MRD clearance	Haplo-HSCT	Alive in remission
5a/M	2 lines of BFM90 TACL.BZ	0.02% 1st relapse	21 days	Yes/No	MRD clearance	Haplo-HSCT	Alive in remission

Abbreviations: BFM, Berlin-Frankfurt-Münster; BFM90, Total XV, Interfant-06, UKALL3, chemotherapy protocols; CR × MRD: complete response with MRD negativity; HSCT, hematopoietic stem-cell transplant; M/F, male/female; MRD, measurable residual disease; PD, progressive disease; PR, partial response; TACL-Bz, Capizzi, IDA-FLAG, salvage regimens.

TABLE 4. Response After the Short-Course Blinatumomab Regimen in Children With Relapsed or Refractory ALL Treated With a Short-Course Blinatumomab Regimen

Response After Blinatumomab	Total, No. (%) 12 (100%)	Relapse/Refractory, No. (%) 8 (66%)	MRD-Positive, No. (%) 4 (33%)
MRD-negative	9 (75)	5 (62.5)	4 (100)
PR with MRD positivity	1 (8.3)	1 (12.5)	0
PD	2 (16.5)	2 (24.5)	0

Abbreviations: MRD, measurable residual disease; PD, progressive disease; PR, partial response.

chemotherapy regimens; four had been previously deemed ineligible for curative therapy at their referring institutions, and two were in second relapse, underscoring the clinical complexity and heavily pretreated nature of this cohort. However, this approach was selectively applied to patients with low leukemic burden (<5% blasts), which might have influenced both response and toxicity outcomes.

The observed response rates and survival outcomes are comparable with those reported in real-world and clinical trial settings. In the RIALTO study, 52% of pediatric patients with R/R ALL achieved CR with undetectable MRD after two 28-day cycles and the 18-month OS was 58%.[18] Similarly, a multicenter cohort reported CR rates of 53% for R/R disease and 62% for MRD persistence after one cycle, with a 2-year OS of 50%.[19] By contrast, the AHOPCA-ALLREC 2014 protocol—applied in LMICs without access to immunotherapy or HSCT—reported a 3-year OS of 36% and an event-free survival of 25%, underscoring the limited efficacy of conventional salvage chemotherapy in such contexts.[20]

A key finding of our study was the remarkably low incidence of treatment-related toxicity, likely influenced by the low leukemic burden at baseline. CRS occurred in 33% of patients, all grade 1 to 2, and resolved with supportive care; no immune effector cell-associated neurotoxicity syndrome (INCANS) or grade ≥3 CRS was observed, and the median hospitalization was only 3 days. These results compare favorably with larger studies, such as the RIALTO trial, where CRS was reported in 20% (1.8% grade ≥3) and INCANS in 41.8%.[18] Structured caregiver education played a pivotal role in ensuring outpatient safety—parents were trained to recognize early signs of CRS and INCANS using a standardized checklist, enabling timely management with hydration, antipyretics, and dexamethasone (10 mg/m²/d, divided every 12 hours) when indicated; tocilizumab was reserved for refractory cases but was not required. This proactive approach likely contributed to the absence of severe toxicities, supporting the feasibility and safety of outpatient immunotherapy in resource-limited settings.

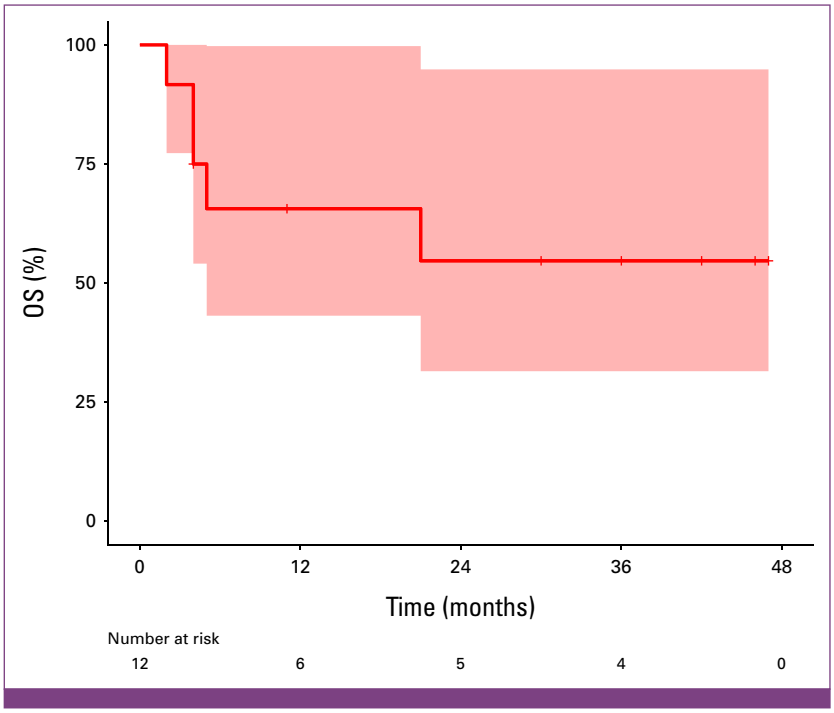

FIG 1. OS in children with relapsed or refractory ALL treated with a short-course blinatumomab regimen followed by hematopoietic stem-cell transplantation. The solid red line represents the Kaplan–Meier estimate of OS for the study cohort, with the shaded area indicating the 95% CI. The risk table shows the number of patients at risk at each time point during follow-up. OS, overall survival.

Infection-related complications were notably absent in our cohort. At our institution, a bortezomib-based reinduction regimen has previously demonstrated an infection rate of 33%[21], whereas dose-adapted chemotherapy protocols in resource-limited settings have reported grade 3 to 4 infections in approximately 25% of patients and an infection-related mortality of 9%. By contrast, no patient in this study developed febrile neutropenia or catheter-related infections although two experienced severe neutropenia. These observations are consistent with larger blinatumomab studies, where documented bacterial infections occurred in only 1.8% of patients and sepsis in 3.6%, underscoring the favorable safety profile of blinatumomab compared with conventional chemotherapy.[18]

Cost optimization played a pivotal role in the feasibility of this intervention. In resource-constrained systems, minimizing waste from high-cost drugs is critical.[14] Through coordinated vial sharing, validated dose optimization, and infusion time adjustments, drug-related expenditures were reduced by 43% without compromising treatment efficacy. Similar experience from China, where shortened 10- to 13-day regimens achieved CR in 83% of patients with R/R ALL and MRD negativity in 40%, supports the potential viability of reduced-duration schedules.[17]

Limited inpatient capacity remains a major barrier to blinatumomab implementation in many Latin American institutions, increasing both cost and logistical burden. In this cohort, 75% of patients completed treatment entirely as outpatients although the need for continuous infusion, home pump management, and 48-hour refills posed challenges. Future strategies such as subcutaneous administration could mitigate these issues. A recent phase I trial from MD Anderson demonstrated that subcutaneous blinatumomab achieved high remission rates (>85%) in heavily pretreated adults with R/R B-ALL, without grade 4 CRS or neurotoxicity, suggesting a promising, practical alternative for future outpatient use once available in Mexico (anticipated by 2028).[22]

This study has several important limitations, including its retrospective design, small sample size, and single-institution scope, which limit the generalizability of the findings. The cost analysis was restricted to drug-related expenditures, excluding hospital personnel, infrastructure, and infusion equipment costs, as these are partially subsidized in our institution. Despite these constraints, the study provides preliminary, hypothesis-generating evidence supporting reduced-duration outpatient blinatumomab as a feasible, context-adapted strategy in resource-limited environments.

A prospective clinical trial is currently ongoing at our center to evaluate 15- and 21-day regimens and is open to enrollment from other institutions without access to blinatumomab. Future collaborative, multicenter studies in Mexico and other LMICs will be critical to validate these findings, assess reproducibility, and determine their broader clinical and economic impact.

Collectively, our results highlight the promise of locally adapted strategies to optimize high-cost therapies, reduce treatment disparities, and promote equitable access to life-saving immunotherapy for children with cancer in resource-constrained settings worldwide.

In conclusion, reduced-duration outpatient blinatumomab may represent a context-adapted strategy with potential cost-savings for pediatric patients with R/R ALL.

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SUPPORT

Supported by AMGEN México through the Blindando Vidas access program, which provided infusion pumps enabling safe outpatient blinatumomab delivery.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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No other potential conflicts of interest were reported.

ACKNOWLEDGMENT

We also thank the CReDO Workshop (International Collaboration for Research Methods Development in Oncology) for its mentorship, which guided the development of our ongoing prospective protocol on dose-optimized, shortened regimens.

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