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RESEARCH ARTICLE

Cost-utility analysis of blinatumomab in pediatric patients with acute lymphoblastic leukemia in Iran

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ABSTRACT

Background and objective: This study aimed to evaluate the cost-utility analyses of blinatumomab in children with relapsed/refractory B-cell Acute Lymphoblastic Leukemia (B-ALL) compared to Consolidation Chemotherapy in Iran.

Method: Based on the results of the phase III randomized 20120215 trial (NCT02393859) the cost-utility analysis, was evaluated over a lifetime using the Parietal Survival model with three health states. The model considered both direct and indirect costs from a societal perspective. The incremental cost-effectiveness ratio (ICER) was calculated by determining the cost per quality-adjusted life year (QALY) gained. Costs and QALYs were discounted annually at 5.8% and 5%, respectively. Deterministic sensitivity analysis (DSA) and Probabilistic sensitivity analysis (PSA) were performed to assess the model's robustness.

Results: The study estimated that blinatumomab is a cost-effective treatment option, with a probability of 57.2%. Blinatumomab was associated with a higher cost ($42,481 versus $21,355) and higher QALYs gained (13.14 versus 8.06) compared to Consolidation Chemotherapy with an ICER of USD 4,160, which is below the willingness-to-pay (WTP) threshold of 4,210 USD in Iran.

Conclusions: Blinatumomab is a cost-effective treatment strategy for pediatric patients with relapsed/refractory B-cell acute lymphoblastic leukemia B-ALL from an Iranian societal perspective.

PLAIN LANGUAGE SUMMARY

This study looked at the costs and benefits of using a medicine called blinatumomab to treat children in Iran who have a difficult-to-treat form of blood cancer called B-cell Acute Lymphoblastic Leukemia (B-ALL). Researchers compared blinatumomab to a standard treatment known as consolidation chemotherapy. Using data from a large clinical trial, they created a model to estimate how much the treatments would cost and how much they would improve patients' lives. The model included both medical costs and other costs that affect families and society. It also measured improvements in health by looking at "quality-adjusted life years," which reflect both how long and how well people live. The results showed that although blinatumomab costs more than the standard treatment, it also helps patients live longer and healthier lives. Overall, the study found that blinatumomab offers good value for money and is a cost-effective option for treating this type of leukemia in children in Iran.

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Cost-utility analysis; economic evaluation; quality-adjusted life years; health economics; precursor cell lymphoblastic leukemia-lymphoma; blinatumomab

1. Introduction

Acute lymphoblastic leukemia (ALL) is a hematologic malignancy marked by the excessive growth of lymphoblasts in the bone marrow and other body areas [1]. It is the most prevalent childhood cancer globally. The average annual incidence of ALL in children under 5 years old in 2021 is 25.66 per 100,000 [2]. The high incidence and prevalence of leukemia significantly contribute to mortality and disease burden, particularly in middle- and low-income countries, where the cost of medication poses a major barrier to effective treatment. ALL accounts for approximately 80% of pediatric leukemias and 20% of adult leukemias. Translocation of chromosomes 9 and 22 (t [3,4], or Philadelphia (Ph) chromosome) leads to expression of the fusion oncogene Bcr-Abl, which produces proteins that act as tyrosine kinases and promote proliferation and survival of tumor cells [5]. Philadelphia chromosome-negative (Ph-) ALL is a genetically heterogeneous disease characterized by recurring cytogenetic or molecular abnormalities contributing to the natural history and overall prognosis [6]. Chemotherapy is the main treatment modality and typically consists of multiple courses of anthracycline, corticosteroids, vincristine, and other combined agents. Most patients treated with chemotherapy have achieved complete remission [5]. Over the past five decades, cure rates for ALL have increased seriously (cure rates currently approaching 90%) [7,8]. However, progress has stalled, as multiple efforts to enhance traditional chemotherapeutic agents have not succeeded in further increasing cure rates [9]. The introduction of tyrosine kinase inhibitors (TKIs) has led to improvements in complete remission rates and overall survival (OS) when added to chemotherapy. It may be useful as maintenance therapy to reduce the risk of relapses after HSCT. While TKIs

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Article highlights

- This study assessed the cost-utility of blinatumomab versus consolidation chemotherapy in children with relapsed/refractory Acute Lymphoblastic Leukemia (ALL) in Iran.
- A lifetime model was applied to a hypothetical cohort of 1,000 patients, incorporating three health states and evaluating both direct and indirect costs from a societal perspective.
- Blinatumomab resulted in higher costs ($42,481 vs. $21,355) but also greater health benefits (13.14 vs. 8.06 QALYs), yielding an ICER of USD 4,160.
- The ICER was below Iran's willingness-to-pay threshold of USD 4,210, indicating cost-effectiveness.
- Sensitivity analyses (DSA and PSA) confirmed the robustness of the model and findings.
- Blinatumomab is a cost-effective treatment strategy for pediatric patients with relapsed/refractory ALL in Iran.

are useful in Ph-positive ALL, there has been a lack of new targeted therapies for Ph-negative disease. Blinatumomab, a bispecific, single-chain molecule designed to engage T cells toward CD19, is a novel agent recently approved by the US Food and Drug Administration for the treatment of relapsed or refractory ALL [5,10]. The approval was based on the 20,120,215 study (NCT02393859) [3]

Considering the disease and economic burden of high-risk First-Relapsed B-ALL in Iran, along with the high efficacy and tolerability of blinatumomab, a targeted monoclonal antibody, this study aims to compare its cost-utility profile to that of Consolidation Chemotherapy for pediatric ALL in Iran. We strive for the findings of this study to offer robust evidence that will guide healthcare decision-making in middle-income countries.

2. Methods

2.1. Model structure

The cost-utility analysis uses a similar model to Caillon et al. [11] and Martinez et al [12]. A partitioned survival model was constructed by TreeAge Pro Healthcare version 2022 R19 software, including three health states: pre-progression state, post-progression state, and death (shown in Figure 1). It is also the most widely used model structure for advanced cancer treatments [13]. Patients were defined to be in the pre-progression state if they had not experienced an event (i.e., relapse, treatment failure relapse, secondary malignancy) or death; patients were in the post-progression state if they had experienced an event and were alive; and patients were in the death state if they had died.

To conduct the cost-utility analysis, we considered treatment outcomes and costs associated with 1 cycle of blinatumomab (15 μg/m^2/d for 4 weeks, continuous intravenous infusion) as a bridge therapy after 2 cycles of consolidation chemotherapy or Consolidation Chemotherapy for the third Consolidation. In this treatment regimen, which was considered a single 2-week cycle, the costs of dexamethasone, vincristine, methotrexate, PEG asparaginase, daunorubicin, ifosfamide, cytarabine, and prednisolone were included [3]. It is noteworthy to mention that PEG asparaginase is one of the primary medications used in Iran. Despite the high cost, which contributes significantly to the overall treatment expenses, PEG asparaginase is an essential component of Consolidation Therapy and cannot be considered optional in routine medical practice in this country. To minimize calculation errors and avoid imposing costs without considering subsequent health outcomes, and based on the oncologist's opinion for patients in the post-progression state, it was assumed that patients would use the FLAG regimen(Chemotherapy regime: Fludarabine+ Cytarabine+ Filgrastim) as maintenance therapy for only one year [14]. Patients in the disease progression state were supposed to receive their treatment regimen during the first week of each month, followed by a three-week rest period; and if the patients died, they would be in a state of death.

Given the nature of the disease, we employed a lifetime horizon of 68 years to encompass all relevant costs and outcomes [15]. The health outcomes were assessed in terms of QALY gained. According to the literature, costs and QALYs were discounted at 5.8% and 5%, respectively [16]. The final result was presented as an incremental cost-effectiveness ratio (ICER), which was then compared against the Iranian WTP threshold range of one Gross Domestic Product (GDP) per capita in 2024, which was 4,210 USD [17]. All aspects of this study were conducted and reported according to the CHEERS checklist (Appendices).

2.2. Model inputs

2.2.1. Clinical efficacy & safety

Based on the Randomized clinical trial 20120215,108 children, older than 28 days and younger than 18 years, were included in

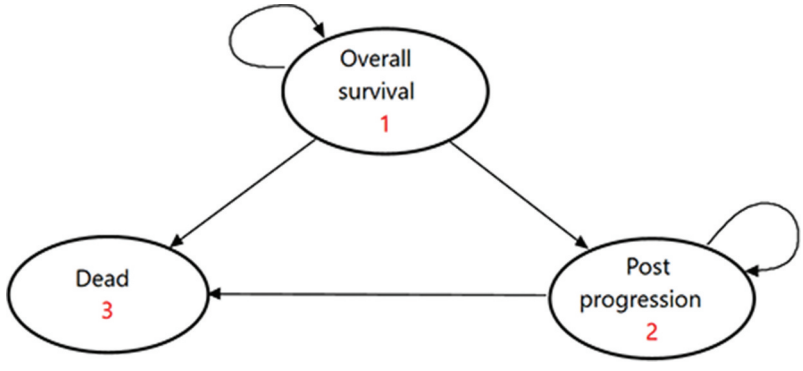

Figure 1. The model structure includes three health states: pre-progression state, post-progression state, and death.

this study and diagnosed with Philadelphia chromosome-negative B-ALL and experiencing a high-risk first relapse. High-risk first relapse was defined as a very early relapse (less than 18 months after the primary diagnosis). Relapse sites include isolated extramedullary, isolated bone marrow, or combined bone marrow/extramedullary sites. Only patients completing induction and the first 2 cycles of standard consolidation therapy were included in the trial. Patients refractory to induction or relapsing during the first 2 blocks of consolidation chemotherapy were excluded. We assumed the same baseline characteristics in our hypothetical cohort as those described in the 20120215 trial [3]. The primary outcomes of this study included progression-free survival (PFS), OS, minimal residual disease (MRD) response, and adverse events. Study data indicated that blinatumomab significantly improved PFS and MRD response rates. The median follow-up time for PFS was 22.4 months, and blinatumomab significantly increased the event-free survival rate compared to chemotherapy. The 24-month survival rate in the blinatumomab group was 66.2%, while it was 27.1% in the chemotherapy group. Additionally, among patients with early relapse, blinatumomab significantly reduced the occurrence of disease events. The median follow-up time for OS was 19.5 months, and the hazard ratio for OS favored blinatumomab. Blinatumomab also improved the complete response rate based on MRD compared to chemotherapy and was associated with fewer serious adverse events. Most patients in the blinatumomab group achieved a complete response, and the relapse rate was lower in this group. Although both treatment regimens had adverse events, blinatumomab generally demonstrated fewer side effects, and severe adverse events such as grade 3 or higher infections were less frequently observed in the blinatumomab group. Since not all patients had relapsed or died by the end of the 20,120,215-study follow-up, event-free survival (EFS) and OS were extrapolated to obtain lifetime estimates of QALYs with Blinatumomab and HC3. The predictions were made by applying parametric survival models to the EFS and OS data at the individual patient level, adhering to the guidelines for survival analysis used in economic evaluations alongside clinical trials [13,18,19].

2.2.2. Resource utilization and costs

Cost estimation was performed from a societal perspective using a micro-costing method. Considering the societal perspective, all direct and indirect costs associated with the disease, including medication, diagnosis, hospitalization, adverse event management, monitoring costs, transportation, palliative care, and the caregiver's costs, considering that the subject of the analysis was a pediatric population, were captured. The data required to estimate costs were gathered from the 20,120,215 trial (such as dosing schedule and average body surface area), national databases (including unit costs and regional tariffs), and expert opinion (to validate assumptions regarding healthcare resource usage and the administration of blinatumomab). Blinatumomab is administered over a 28-day cycle, followed by a 14-day treatment-free interval. The administration protocol typically involves an initial inpatient period to monitor adverse reactions, with subsequent treatment potentially transitioning to an outpatient setting. According to expert opinions, it was assumed that patients received blinatumomab via intravenous infusion on an inpatient basis for the initial 3 days, transitioning to outpatient care for the rest of the cycle, with infusion bag changes occurring every 3 days. To accurately reflect real-world practice, blinatumomab wastage was considered in the base-case analysis. Since opened vials have a limited storage time and the number of patients eligible for Blinatumomab therapy, hospitals are unlikely to reuse the contents of opened vials [20]. Caregiver-related costs included productivity loss, estimated based on the time caregivers spent in the hospital (approximately 15 days), assuming one caregiver accompanied the child during each hospital stay estimated based on the minimum daily wage in Iran, which was 12.6 USD. The study's clinical advisor validated all direct and indirect healthcare cost assumptions. The costs are collected in Iranian Rial currency, but all costs were presented in USD with an exchange rate of 1 USD = 285,000 Iranian Rials (Table 1).

2.2.3. Utilities

Health-related quality of life (HRQoL) was not assessed in the 20,120,215 trial; therefore, data from the phase III randomized TOWER trial, which compared blinatumomab ($n = 271$) with standard-of-care (SOC) chemotherapy ($n = 134$) in adult patients with relapsed/refractory B-ALL, were utilized [21]. During the first cycle, utility values for patients receiving blinatumomab (or HC3) were assumed to match those of patients receiving blinatumomab (or SOC chemotherapy) in the TOWER trial. In subsequent cycles, utility values were considered uniform across treatment arms within each health state. For patients surviving beyond five years, utility values were modeled to approach general population norms gradually, with those who stayed for 25 years assumed to have the same utility levels as the general population. No specific disutility was applied for adverse events. However, disabilities related to HSCT and graft-versus-host disease (GVHD) were included, based on Furlong et al. [22]. The negative impact of pediatric ALL on parental HRQoL was also included in their analysis from a societal perspective. Ultimately, for the first five years of the study, quality of life was considered 0.77 and 0.59 for patients in pre-progression and post-progression health states, respectively. In this study, patient quality of life in various health states was also considered, similar to the cost-effectiveness study by Caillon et al. [11].

2.3. Sensitivity analysis

To address uncertainties in the study, both DSA and PSA were conducted to examine the robustness of the model results. A tornado diagram was generated to illustrate the sensitivity levels of parameters, ranging from most to least sensitive within a ±20% interval. This involved systematically altering critical parameters to assess their impact on the model's outcomes. To evaluate the uncertainty of all parameters. Simultaneously, a PSA was conducted using a second-order Monte Carlo simulation.

3. Results

The model output indicated that patients in the blinatumomab group had a higher probability of OS and PFS than the Consolidation Chemotherapy group. The model's predictions show that patients who survive the fifth year after starting

Table 1. Summary of key model parameters.

Parameter	Point estimate	Distribution	Values tested in the DSA	References
Analytic variables				
Time horizon	Lifetime (approximately 68 years)	NA	NA	[15]
Annual discount rate	5% for QALY 5.8% for costs	NA	NA	[16]
Patient characteristics				
Body Surface Area (Mean)	0.95	Normal	0.87–1.03	[3]
Starting age	7 years	Normal	6.2–7.8	[3]
Weight	23.7 kg	Normal	24.5–30.1	[3]
Blinatumomab administration				
Dose on days1-28	14.25 µg	Normal	13.20–28	[3]
Bag change	Every 3 days	Normal	3.5–4	[3]
Costs (USD)				
Adverse event Blinatumomab	396.4	Gamma	±20	
Adverse event chemotherapy	800.5	Gamma	±20	
FLAG	1315.3	Gamma	±20	
GVHD	2980.3	Gamma	±20	
HSCT	6202.5	Gamma	±20	
Immunosuppressive	791.8	Gamma	±20	
Induction Blinatumomab	29,716	Gamma	±20	
Induction chemotherapy	3747.7	Gamma	±20	
Probabilities				
GVHD	0.059	Beta	±20	[3]
HSCT Blinatumomab	0.889	Beta	±20	[3]
HSCT chemotherapy	0.704	Beta	±20	[3]
24-month survival rate	Blinatumomab:66.2% Chemotherapy:27.1%		±20	[3]
Median follow-up time for overall survival	19.5 months		±20	[3]
Median follow-up time for progression-free survival	22.4 month		±20	[3]
Utilities				
Cycle 1, progression-free health state	Blinatumomab: 0.77 chemotherapy: 0.66	Beta	±20	[4]
Cycle 2 or higher, progression-free health state	Blinatumomab: 0.77 chemotherapy: 0.77	Beta	±20	[4]
post-progression health state	Blinatumomab: 0.59 Chemotherapy: 0.59	Beta	±20	[4]

Abbreviations: DSA: deterministic sensitivity analysis; FLAG: Chemotherapy regimen (Fludarabine, Cytarabine, Filgrastim); GVHD: graft-versus-host disease; HSCT: hematopoietic stem cell transplantation.
This table provides a summary of key model parameters and their point estimate, distributions, values tested in DSA and the references for indicated data.

treatment follow the natural mortality rate. Additionally, considering the life expectancy in Iran (an average of 75 years) and the age of patients at the start of the study (an average of 7 years), patients were followed and modeled for up to 816 monthly cycles (68 years) (shown in Figure 2).

3.1. Base-case result

When considering a lifetime horizon, the QALYs associated with blinatumomab and chemotherapy were estimated to be 13.14 years and 8.06 years, respectively (as detailed in Table 2). The total costs related to blinatumomab and chemotherapy were 42,481 USD and 21,355 USD, respectively. The cost of blinatumomab was 1859.6 USD per 35 mg vial, which was associated with an average increase of 21,126 USD in treatment costs and a gain of 5.08 QALYs per patient. The base-case model's results indicated that blinatumomab is a cost-effective option in Iran with an ICER of 4,160 USD and a WTP threshold of 4,210 USD.

3.2. Sensitivity analyses

3.2.1. DSA

As shown in Figure 3, the model was sensitive to changes in five key variables: the price of a vial of Blinatumomab, the exchange rate of Iranian Rial(IRR), the discount rate for effectiveness, the quality-of-life rates for patients in pre-progression and post-progression states, and the probability of HSCT for patients in the Consolidation Chemotherapy group.

For instance, as shown in Figure 4 if the price of blinatumomab exceeds 1,878 USD per 35-mg vial, the drug would no longer be cost-effective.

3.2.2. PSA

The PSA was conducted by incorporating key study variables as random variables with appropriate distributions for each variable, using the Monte Carlo method with 1,000 random iterations. This analysis indicated that blinatumomab was cost-effective in 57.2% of cases (shown in Figure 5).

4. Discussion

This study evaluates the cost-effectiveness of blinatumomab compared to Consolidation Chemotherapy for pediatric patients with high-risk, First-Relapsed B-ALL in Iran. The findings indicate that blinatumomab is a clinically effective treatment option and a cost-effective strategy from a societal perspective.

The total cost of blinatumomab is higher compared to chemotherapy (42,481 USD vs. 21,355 USD), which is mostly attributed to the higher price of the drug and a greater proportion of patients who could receive expensive HSCT [11]. Taking both the benefits and costs into account, blinatumomab proved to be a cost-effective alternative to chemotherapy. Its ICER was estimated at 4,160 USD per QALY gained, which falls below Iran's WTP of one GDP per capita (4,210 USD). PSA indicated that blinatumomab was cost-effective in

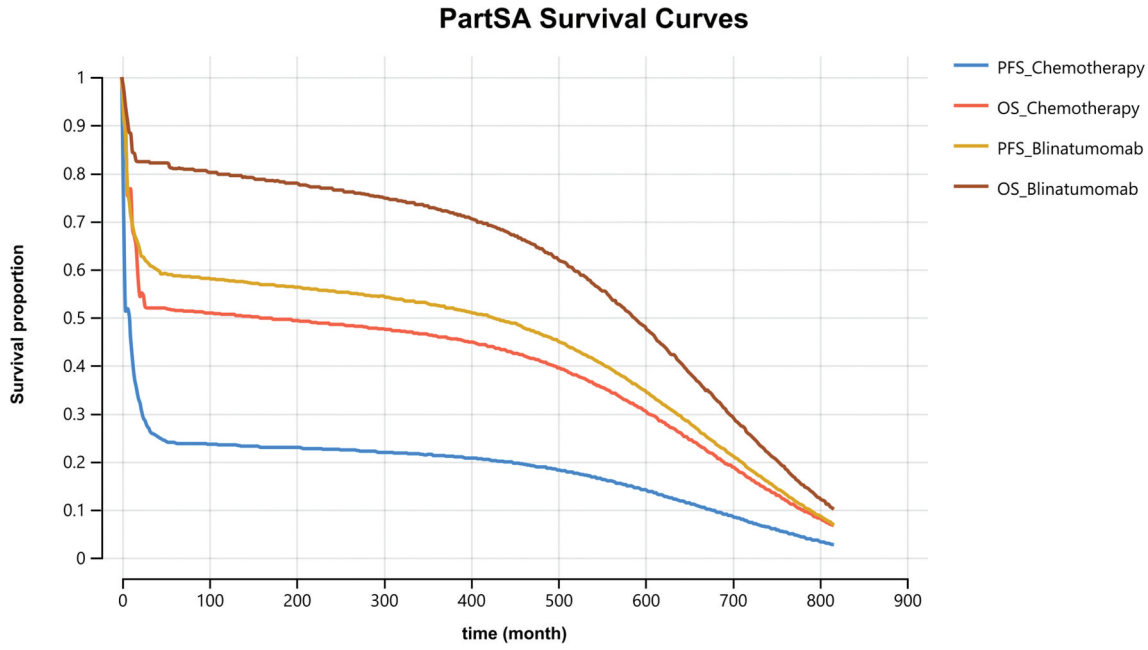

Figure 2. Survival analysis curve of patients demonstrates that patients in blinatumomab group had a higher probability of OS and PFS than SOC. If the patients survive for 5 years after starting their treatment, they will follow natural mortality rate.

Table 2. Base-case model results.

strategy	Cost (USD)	Incremental Cost	Effectiveness (QALY)	Incremental Effectiveness	ICER(USD/QALY)
Chemotherapy	21,355		8.06		
Blinatumomab	42,481	21,126	13.14	5.08	4,160

Abbreviations: ICER: Incremental cost-effectiveness ratio, QALY: Quality-adjusted life year.
This table summarize and compare the cost, incremental cost, effectiveness and Incremental effectiveness of the two arms of the study. This model showed that blinatumomab is a cost-effective option in Iran with an ICER of 4,160 USD and a WTP threshold of 4,210 USD.

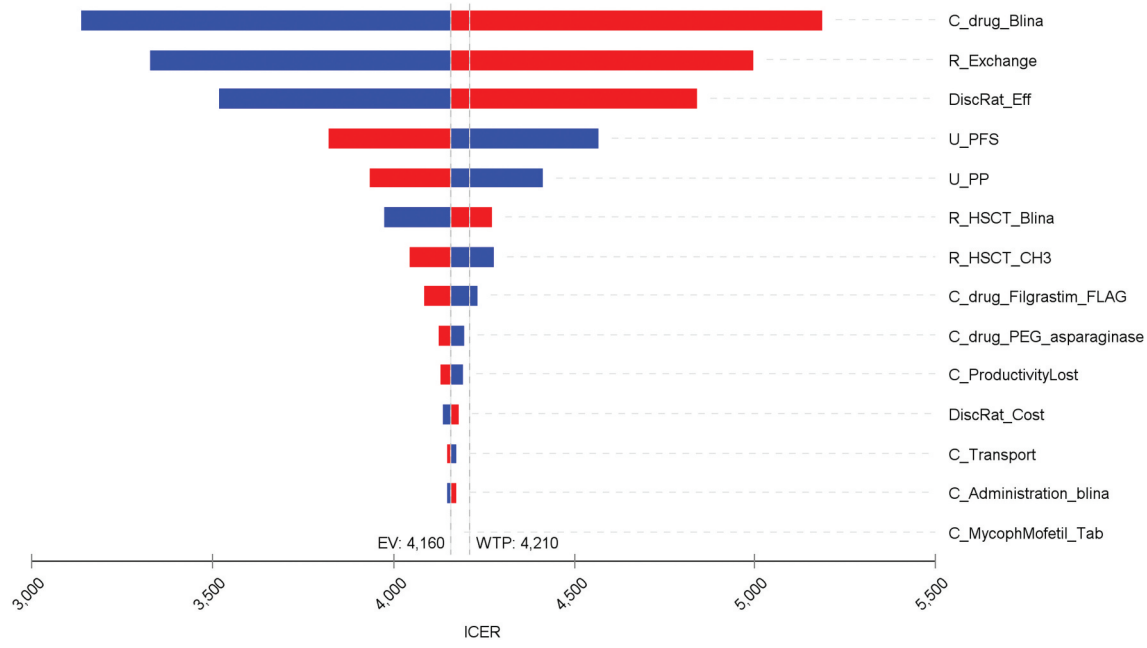

Figure 3. This tornado diagram shows that the model was sensitive to changes in the price of a vial of blinatumomab, the exchange rate of Iranian Rial (IRR), the discount rate for effectiveness, the quality-of-life rates for patients in pre-progression and post-progression states, and the probability of HSCT for patients in the Consolidation chemotherapy group.

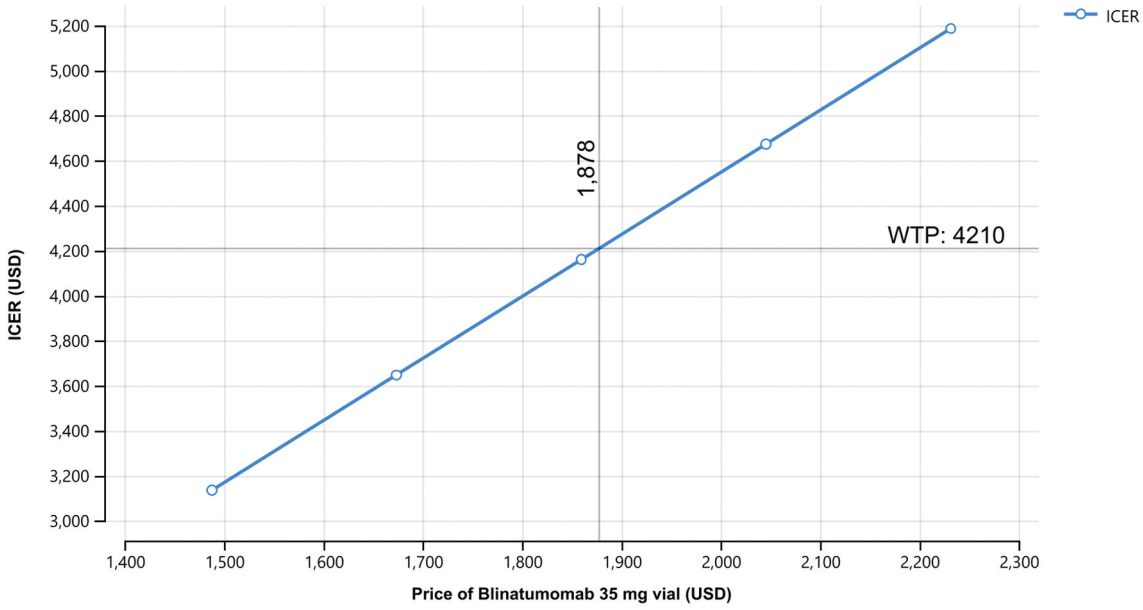

Figure 4. This figure explores the relationship between the price of blinatumomab and ICER. The intersection of the ICER curve and the WTP threshold occurs at a blinatumomab price of approximately $4,210 per vial. This suggests that at prices above $4,210, the drug may no longer be considered cost-effective compared to SOC chemotherapy.

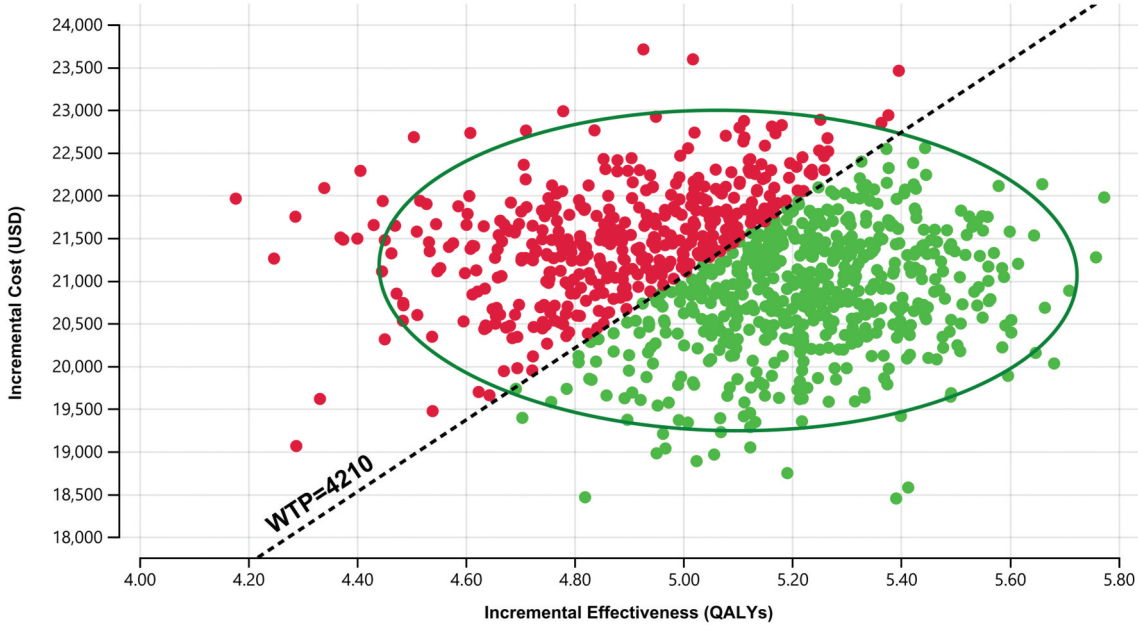

Figure 5. The Monte Carlo sensitivity analysis showed that blinatumomab was cost-effective in 57.2% of cases.

57% of resampling scenarios. This indicates that the higher costs of blinatumomab are offset by the significant health benefits it offers.

In evaluating the DSA, the tornado analysis showed that the used model is not sensitive to input parameters; the most notable variations occurred when varying the price of a vial of blinatumomab, the exchange rate of IRR, and the discount rate for effectiveness. The cost-effectiveness of blinatumomab was significantly influenced by the annual discount rates of 5% for QALYs and 5.8% for costs. Reducing these rates would further improve its cost-effectiveness by lowering the present value of future costs, strengthening its economic justification. To the best of our knowledge, this is the first cost-effectiveness evaluation of blinatumomab in pediatric patients with high-risk first relapse of ALL conducted in Iran. Our study utilizes a decision-analytic model similar to those employed by Caillon et al. in France [11] and Martinez et al. in Mexico [12], with several methodological adaptations to reflect local clinical and economic conditions.As previously noted, a study conducted in France supports the use of blinatumomab as a valuable therapeutic option for ALL, considering both healthcare and societal perspectives. In that study, blinatumomab was associated with an additional 7.16 QALYs compared to chemotherapy (19.77 vs. 12.62), albeit with higher total costs (€154,326 vs. €102,028).

In contrast, our analysis estimated a lower QALY gain of 5.08 (13.14 vs. 8.06), alongside higher total costs (USD 42,481 vs. USD 21,355). The ICER in the French study was €7,308 per QALY gained, well below France's informal WTP threshold of €150,000, indicating a 99% probability of cost-effectiveness. Meanwhile, the ICER in Iran was estimated at USD 4,160 per QALY, slightly below the national WTP threshold of USD 4,210, with a 57% probability of cost-effectiveness.

It is important to note that the French study applied a discount rate of 2.5% for the first 30 years and 1.5% thereafter, whereas our national guidelines recommend discount rates of 5% for QALYs and 5.8% for costs. These methodological differences likely contributed to the variation in outcomes between the two studies [11].

However, In Mexican cost-effectiveness study conducted from a healthcare perspective estimated the total discounted life-years (LYs) for blinatumomab and consolidation chemotherapy at 14.9 years and 9.79 years, respectively. The associated total costs were $1,952,966 MXN for blinatumomab and $1,331,855 MXN for chemotherapy. These figures yielded an incremental cost-effectiveness ratio (ICER) of $121,536 MXN per LY gained, well below Mexico's informal WTP threshold, which ranges from $200,000 to $600,000 MXN. Sensitivity and scenario analyses reinforced the robustness of these results, with cost-effectiveness probabilities exceeding 85% even under conservative assumptions. According to Mexican health technology assessment (HTA) guidelines, an annual discount rate of 5% was applied to both costs and future health outcomes [12]. Another study using population-based healthcare data from Ontario, Canada, indicated that blinatumomab was associated with an average higher life expectancy (43.4 years vs. 36.8 years) and 2.75 QALYs gained but higher costs (60,420 CAD) compared to standard intensive chemotherapy [4]. This consistency across different geographic and economic settings strengthens the argument for incorporating blinatumomab into standard treatment protocols for high-risk pediatric ALL.

The indication for blinatumomab is not restricted to pediatric ALL. Studies have demonstrated that blinatumomab is also effective in adults with ALL [6]. A study conducted in the United States by Delea et al. evaluates the cost-effectiveness of blinatumomab (Blincyto) versus the SOC for adults with relapsed/refractory Philadelphia-chromosome-negative B-precursor ALL from a US healthcare payer perspective, using data from the phase 3 TOWER study. A partitioned survival model estimated the ICER. blinatumomab was projected to provide 1.92 additional life years and 1.64 additional quality- QALYs at an incremental cost of $180,642, resulting in an ICER of $110,108/QALY. The cost-effectiveness was impacted by hospitalization expenses and previous salvage treatment. At an ICER threshold of $150,000/QALY, blinatumomab had a 74% probability of being cost-effective. According to the study's findings, blinatumomab is a cost-effective option relative to SOC in this particularly difficult-to-treat patient population [23].

In 2022, Ranin Soliman systematically reviewed the costs and cost-effectiveness of treatments for relapsed/refractory ALL in children. The study concluded that while chimeric antigen receptor (CAR)-T cell therapy is a cost-effective yet novel approach for relapsed/refractory ALL, concerns remain regarding its long-term effectiveness, affordability, and accessibility. Blinatumomab and Clofarabine offer better value compared to FLA-IDA chemotherapy (Chemotherapy regimen: Fludarabine + Cytarabine + Idarubicin). The evidence quality ranges from moderate to high, though generalizability is limited due to variability in outcomes from modeling studies [24].

Iran's healthcare system is characterized by a fragmented insurance structure and mixed financing mechanisms, including government subsidies, social insurance, and significant out-of-pocket payments. Despite over 90% of the population being covered by some form of health insurance, disparities in benefit packages and reimbursement policies persist across different schemes, such as the Social Security Organization and the Iran Health Insurance Organization. The Health Transformation Plan (HTP), launched in 2014, aimed to improve financial protection and access to care, yet challenges remain – particularly in achieving equity and sustainability. High out-of-pocket expenditures, which account for nearly 40% of total health spending, continue to expose households to financial hardship. These systemic factors directly influence the affordability and cost-effectiveness of high-cost treatments like blinatumomab and must be considered when interpreting results and assessing generalizability within Iran's economic and policy landscape [25].

The present study is subject to some limitations. First, the study analysis relies on a partitioned survival model, which, while useful for estimating outcomes over time, does not capture the complex interdependence between key clinical events such as treatment response, relapse, allogeneic stem cell transplantation (alloHSCT), and overall survival. Our model incorporated long-term survival data from the pivotal trial and comparable studies, which consistently showed a plateau in survival curves [26,27]. However, extrapolating survival involves assumptions that introduce uncertainty. Despite using the best available evidence and expert input, real-world outcomes may differ due to factors not fully captured in the model. Second, the 20,120,215 trial did not assess health-related quality of life (HRQoL); children under 6–7 years old can't describe their pain properly. Similar to the French study, to estimate the quality of life, we used data from other studies with older patients [28].

The economic burden of pediatric cancers, particularly leukemias, calls for the adoption of cost-effective treatments that can enhance patient outcomes without overwhelming healthcare budgets. The favorable cost-effectiveness profile of blinatumomab supports its incorporation into standard treatment protocols for high-risk pediatric ALL. By prioritizing such therapies, healthcare systems can optimize resource allocation, ensuring that investments lead to meaningful health improvements. The results of this study have significant implications for healthcare decision-makers in Iran and similar middle-income countries.

Although this analysis provides strong support for Blinatumomab's cost-effectiveness, further research is needed to investigate potential variations among different populations and compare Blinatumomab with other treatments. Future studies could also evaluate Blinatumomab's effect on other health outcomes, such as the long-term psychological effects of treatment on patients and caregivers.

5. Conclusion

From a societal perspective, blinatumomab proved to be a cost-effective treatment option compared to Consolidation Chemotherapy with an ICER below the Iranian WTP threshold. Decision-makers can use these results to optimize treatment pathways, improve patient outcomes, and allocate healthcare resources efficiently.

Author contributions

Idea generation: BF, AE; methodological design: BF; data gathering: BF; analysis: BF; drafting and manuscript preparation: GN, ZA; revision: BF, AE; final approval, confirmation, and critical appraisal: AE, BF, GN.

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References

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.

1. Jabbour EJ, Faderl S, Kantarjian HM. Adult acute lymphoblastic leukemia. Mayo Clin Proc. 2005;80(11):1517–1527. doi: 10.4065/80.11.1517
2. Ding F, Deng L, Xiong J, et al. Analysis of global trends in acute lymphoblastic leukemia in children aged 0–5 years from 1990 to 2021. Front Pediatr [Internet]. 2025;13(March):1–11. doi: 10.3389/fped.2025.1542649
3. Locatelli F, Zugmaier G, Rizzari C, et al. Effect of blinatumomab vs chemotherapy on event-free survival among children with high-risk first-relapse B-cell acute lymphoblastic leukemia: a randomized clinical trial. JAMA [Internet]. 2021 Mar 2;325(9):843–854. doi: 10.1001/jama.2021.0987
   - **This article is a randomized clinical trial assessing the effectiveness of Blinatumomab compared to chemotherapy. The results from this study provided essential clinical data for our analysis.**
4. Pechlivanoglou P, Luu L, Li Q, et al. Blinatumomab is cost-effective compared to standard chemotherapy for children with high risk relapses of acute lymphoblastic leukemia: a cost-effectiveness analysis using population-based healthcare data. Blood. 2021;138(Supplement 1):565–565. doi: 10.1182/blood-2021-154193
   - **The following article provided Health-Related Quality of Life (HRQoL) of Blinatumomab Versus Standard of Care (SOC) Chemotherapy data which were crucial for our study's evaluation of the cost-utility of Belinatumomab.**
5. Newman MJ, Benani DJ. A review of blinatumomab, a novel immunotherapy. J Oncol Pharm Pract. 2016;22(4):639–645. doi: 10.1177/1078155215618770
6. Burkart M, Dinner S. Advances in the treatment of Philadelphia chromosome negative acute lymphoblastic leukemia. Blood Rev. 2024;66:101208. doi: 10.1016/j.blre.2024.101208
7. Pui CH, Yang JJ, Hunger SP, et al. Childhood acute lymphoblastic leukemia: progress through collaboration. J Clin Oncol [Internet]. 2015 Aug 24;33(27):2938–2948. doi: 10.1200/JCO.2014.59.1636
8. Nakata K, Ito Y, Magadi W, et al. Childhood cancer incidence and survival in Japan and England: a population-based study (1993–-2010). Cancer Sci. 2018;109(2):422–434. doi: 10.1111/cas.13457
9. Gupta S, Rau RE, Kairalla JA, et al. Blinatumomab in standard-risk B-cell acute lymphoblastic leukemia in children. N Engl J Med. 2024;392(9):1–16. doi: 10.1056/NEJMoa2411680
10. Elitzur S, Arad-Cohen N, Barzilai-Birenboim S, et al. Blinatumomab as a bridge to further therapy in cases of overwhelming toxicity in pediatric B-cell precursor acute lymphoblastic leukemia: report from the Israeli study group of childhood leukemia. Pediatr Blood Cancer. 2019;66(10):1–6. doi: 10.1002/pbc.27898
11. Caillon M, Brethon B, van Beurden-Tan C, et al. Cost-effectiveness of blinatumomab in pediatric patients with high-risk first-relapse B-cell precursor acute lymphoblastic leukemia in France. Pharmacoecon Open. 2023;7(4):639–653. doi: 10.1007/s41669-023-00411-4
    - **The following articles had similar approches for the cost-effectiveness analysis of belinatomomab in Pediatric Patients with High-Risk First-Relapse B-Cell Precursor Acute Lymphoblastic Leukemia in France and Mexico. Theses studies were helpful not only in designing our model but in facilitating a comparison of results.**
12. Diaz Martinez JP, de Maraumont TA, Camacho LM, et al. Cost-effectiveness of blinatumomab for the treatment of B-precursor acute lymphoblastic leukemia pediatric patients with high-risk first-relapse in Mexico. Leuk Res. 2024;145(July):107560. doi: 10.1016/j.leukres.2024.107560
    - **The following articles had similar approches for the cost-effectiveness analysis of belinatomomab in Pediatric Patients with High-Risk First-Relapse B-Cell Precursor Acute Lymphoblastic Leukemia in France and Mexico. Theses studies were helpful not only in designing our model but in facilitating a comparison of results.**
13. Woods B, Sideris E, Palmer S, et al. NICE DSU technical support document 19. Partitioned Survival Analysis for Decision Modelling in Health Care: A Critical Review. 2017. Available from: https://sheffield.ac.uk/nice-dsu
14. Brown P, Inaba H, Annesley C, et al. Pediatric acute lymphoblastic leukemia, version 2.2020, NCCN clinical practice guidelines in oncology. J Natl Compr Cancer Netw. 2020;18(1):81–112. doi: 10.6004/jnccn.2020.0001
15. Ebrahimi N, Mehdipour P, Mohebi F, et al. Improved population health in Iran from 1979 to 2019; decreasing mortality rates and increasing life expectancy. Arch Iran Med. 2020;23(2):61–68.
16. Daneshmand A, Jahangard E, Abdollah-Milani M. A time preference measure of the social discount rate for Iran. J Econ Struct. 2018;7(1). doi: 10.1186/s40008-018-0127-x
17. Bertram MY, Lauer JA, De Joncheere K, et al. Policy & practice cost–effectiveness thresholds: pros and cons thresholds based on gross domestic product. Bull World Heal Organ. 2016;94(July):925–930.
    - **Lastly, we required the discount rates for the comparison of costs and benefits occurring at different times which is a critical aspect of health economic studies. This information was provided by the following article.**
18. Latimer NR. Survival analysis for economic evaluations alongside clinical trials–extrapolation with patient-level data: inconsistencies, limitations, and a practical guide. Med Decis Mak. 2013 Aug;33(6):743–754. doi: 10.1177/0272989X12472398

19. Rutherford M, Lambert P, Sweeting M, et al. Nice DSU technical support document 21: flexible methods for survival analysis. Leicester, (UK): Dep Heal Sci Univ Leicester; 2020 Jan. p. 1–97.
20. European Medicines Agency. Blincyto - summary of product characteristic. 2020. p. 193–214.
21. Kantarjian H, Stein A, Gökbuget N, et al. Blinatumomab versus chemotherapy for advanced acute lymphoblastic leukemia. N Engl J Med. 2017;376(9):836–847. doi: 10.1056/NEJMoa1609783
22. Furlong W, Rae C, Feeny D, et al. Health-related quality of life among children with acute lymphoblastic leukemia. Pediatr Blood Cancer. 2012;59(4):717–724. doi: 10.1002/pbc.24096
23. Delea TE, Amdahl J, Boyko D, et al. Cost-effectiveness of blinatumomab versus salvage chemotherapy in relapsed or refractory Philadelphia-chromosome-negative B-precursor acute lymphoblastic leukemia from a US payer perspective. J Med Econ. 2017;20(9):911–922. doi: 10.1080/13696998.2017.1344127
24. Soliman R, Heneghan C, Bolous NS, et al. Systematic review of costs and cost-effectiveness of treatment for relapsed/refractory acute leukemia in children and young adults. Expert Rev Hematol. 2022;15(4):345–357. doi: 10.1080/17474086.2022.2069096
25. Doshmangir L, Bazyar M, Rashidian A, et al. Iran health insurance system in transition: equity concerns and steps to achieve universal health coverage. Int J Equity Health. 2021;20(1):1–14. doi: 10.1186/s12939-020-01372-4
26. Nguyen K, Devidas M, Cheng SC, et al. Factors influencing survival after relapse from acute lymphoblastic leukemia: a children's oncology group study. Leukemia. 2008 Dec;22(12):2142–2150. doi: 10.1038/leu.2008.251
27. Einsiedel HG, von Stackelberg A, Hartmann R, et al. Long-term outcome in children with relapsed ALL by risk-stratified salvage therapy: results of trial acute lymphoblastic leukemia-relapse study of the Berlin-Frankfurt-Münster group 87. J Clin Oncol Off J Am Soc Clin Oncol. 2005 Nov;23(31):7942–7950. doi: 10.1200/JCO.2005.01.1031
28. Topp MS, Zimmerman Z, Cannell P, et al. Health-related quality of life (HRQoL) of blinatumomab versus standard of care (SOC) chemotherapy in patients with relapsed or refractory Philadelphia negative B-cell precursor acute lymphoblastic leukemia in a randomized, open-label phase 3 study (TOWER). Blood. 2016;128(22):222–222. doi: 10.1182/blood.V128.22.222.222