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Cost-Effectiveness of Chimeric Antigen Receptor T-Cell Therapy in Pediatric Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia

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Abstract

Background: Chimeric antigen receptor T-cell (CAR-T) therapy is a promising new class of cancer therapy but has a high up-front cost. We evaluated the cost-effectiveness of CAR-T therapy among pediatric patients with relapsed/refractory B-cell acute lymphoblastic leukemia (B-ALL).
Methods: We built a microsimulation model for pediatric patients with relapsed/refractory B-ALL receiving either CAR-T therapy or standard of care. Outcomes included costs, quality of life (health utility), complications, and survival. We measured cost-effectiveness with the incremental cost-effectiveness ratio (ICER), with ICERs under $100 000 per quality-adjusted life-year (QALY) considered cost effective. One-way and probabilistic sensitivity analyses were used to test model uncertainty.
Results: Compared to standard of care, CAR-T therapy increased overall cost by $528 200 and improved effectiveness by 8.18 QALYs, resulting in an ICER of $64 600/QALY. The model was sensitive to assumptions about long-term CAR-T survival, the complete remission rate of CAR-T patients, and the health utility of long-term survivors. The base model assumed a 76.0% one-year survival with CAR-T, although if this decreased to 57.8%, then CAR-T was no longer cost effective. If the complete remission rate of CAR-T recipients decreased from 81% to 56.2%, or if the health utility of disease-free survivors decreased from 0.94 to 0.66, then CAR-T was no longer cost effective. Probabilistic sensitivity analysis found that CAR-T was cost effective in 94.8% of iterations at a willingness to pay of $100 000/QALY.
Conclusion: CAR-T therapy may represent a cost-effective option for pediatric relapsed/refractory B-ALL, although longer follow-up of CAR-T survivors is required to confirm validity of these findings.

The outcomes for pediatric B-cell acute lymphoblastic leukemia (B-ALL) patients overall have improved substantially over the past several years, with 10-year survival rates increasing from 69.3% in 1981 to 85.5% in 2010 (1–5). Despite this success, outcomes for the subset of patients who relapse or are refractory to initial treatment remain exceedingly poor. Until recently, no clear standard therapy existed for relapsed/refractory B-ALL patients, and, in general, patients enrolled into clinical trials or received intensified treatment with conventional agents not used in their first course of therapy (6). Unfortunately, with conventional therapy the 10-year overall survival has remained steady at around 30% for the past several years (7,8).

Recently, the development of anti-CD19 chimeric antigen receptor T-cell (CAR-T) therapy has led to increased optimism for patients with relapsed or refractory ALL (9). CAR-T therapy involves collection of a patient's T cells, which are genetically engineered to express activating receptors directed against antigens expressed by the patient's tumor cells and infused back into the patient. A single-center phase I/II study among pediatric patients with CD19+ relapsed or refractory ALL treated with tisagenlecleucel found a complete remission rate of 93% (10). An additional, more recent multi-institutional phase II study by Maude et al. (11) found an 81% remission rate and 76% overall survival at 1 year.

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CAR-T therapy has generated excitement surrounding its clinical potential, but has also gained attention because of the high up-front cost of treatment (12). A single dose of CAR-T therapy can cost up to $475 000. Additionally, despite the clinical efficacy, CAR-T therapy can evoke an immune response, called cytokine release syndrome, that requires hospitalization, intensive care unit admission, and long-term medications that can further increase the cost of care (13,14). The potential clinical benefits of CAR-T therapy coupled with its high cost raise the issue of cost-effectiveness. At a time when health-care costs are rising exponentially (15), determining the value of new classes of therapy is of utmost importance. The purpose of this study was to analyze the cost-effectiveness of CAR-T therapy compared with standard therapy for pediatric patients with relapsed/refractory B-ALL.

Methods

Cost-Effectiveness Model

We developed an individual-based state-transition microsimulation model to simulate the clinical course of 100 000 pediatric patients with relapsed/refractory B-ALL who received either CAR-T therapy or standard of care. The microsimulation model incorporated costs, toxicity, quality of life, disease progression, and survival for simulated patients. We used a 1-month cycle length, and the simulation extended over the entire life of the patient. Microsimulation models have practical advantages over conventional Markov models in that they more readily simulate numerous health states, and also track an individual patient's history. These features of microsimulation models permit more complex and computationally feasible model design (16). The microsimulation model was constructed with TreeAge Pro 2017 (TreeAge Software, Williamstown, MA).

Patient Population and Treatment

The state-transition diagram (Figure 1) depicts how simulated patients moved through the microsimulation model. All patients started in the treatment health state, and could enter remission, suffer recurrence or progression, or die. Additionally, patients could experience acute and long-term toxicity attributable to their disease (described in detail below). The standard (base-case) patient was a 12-year-old boy weighing 40 kg, with a body surface area of 1.4 m^2. We derived model inputs from the literature to help model the risks of disease recurrence, toxicity, and survival for patients treated with CAR-T and standard of care therapy (11,17,18). For patients treated with CAR-T therapy, we modeled outcomes after the recent phase II study by Maude et al. (11), which included pediatric relapsed/refractory B-ALL patients treated with the anti-CD19 CAR-T therapy tisagenlecleucel. Patients in the CAR-T simulation group were assumed to have received lymphodepleting chemotherapy (fludarabine 30 mg/m^2 intravenously daily for 4 doses and cyclophosphamide 500 mg/m^2 intravenously daily for 2 doses) followed by CAR-T infusion (18). Patients who responded to CAR-T therapy were given intravenous immunoglobulin G (IVIG) infusion monthly for 18 months to treat B-cell aplasia, although this number was varied widely in our sensitivity analysis given that the required duration of IVIG remains unknown (11). Patients who failed to respond to CAR-T therapy received the standard-of-care arm treatment as salvage. The standard-of-care arm was modeled after a phase II trial by Hijiya et al. (17), where patients received up-front clofarabine (40 mg/m^2 daily for 5 doses), etoposide (100 mg/m^2 daily for 5 doses), and cyclophosphamide (440 mg/m^2 daily for 5 doses), followed by hematopoietic stem cell transplantation (HSCT) among responders. We assumed that if a patient survived for 2 years then they had experienced a "successful" HSCT, and we varied this successful HSCT threshold assumption in our sensitivity analysis. Our base-case model followed the Maude trial in that we did not require CAR-T responders to undergo a HSCT, although the role of HSCT after CAR-T is not entirely clear; therefore we tested this assumption in our sensitivity analysis. We estimated response rates directly from the Maude and Hijiya trials. Supplementary Table 1 (available online) shows baseline demographic and clinical characteristics of the patients in these trials.

Model inputs including transition probabilities, costs, and health utilities are included in Table 1, and described further below.

Model Transition Probabilities

We hypothesized that our cost-effectiveness model would be sensitive to assumptions about survival, even though with the novelty of CAR-T therapy and lack of long-term clinical trial follow-up we lack data about long-term survival in responders. Therefore, we estimated the long-term survival of this population under a range of different assumptions described briefly below and described in more detail in the Supplementary Methods (available online). Our base-case survival estimate incorporated long-term survival information from the Surveillance, Epidemiology, and End Results database and mortality information collected by the US Social Security Administration. In addition to this base-case survival estimate, we modeled multiple alternative survival scenarios including an "optimistic" model, a "pessimistic" model, and a "fixed annual mortality" model. Finally, the Hijiya trial included only 25 patients; therefore we conducted an additional sensitivity analysis using retrospective data from two additional, single-arm "standard therapy" studies [the Locatelli et al. trial (19) and the Miano et al. trial (20)] in place of the Hijiya trial.

With respect to toxicity, we used clinical trial data to infer rates of toxicities including cytokine release syndrome, intensive care unit admission, infection, and hematologic toxicities. Patients can experience acute toxicity concurrently with the remission or disease progression health states. We allowed patients to experience toxicity related to long-term treatment for up to 10 years after treatment, although we varied this assumption in our sensitivity analyses.

Costs

The costs of systemic agents were estimated from the average wholesale price (21–26) with a standard 7% reduction (27). For tisagenlecleucel, we followed the outcomes-based reimbursement approach set forth by the manufacturer where payment is required only for those who respond to the drug (28). We held the cost of tisagenlecleucel constant for analysis with both the payer and societal perspectives. The costs of toxicity were taken from previously published literature (29–36). Patients who died after disease relapse incurred the cost of end-of-life care in the month in which they died (35).

All costs were adjusted to 2017 dollars via the Consumer Price Index to account for inflation.

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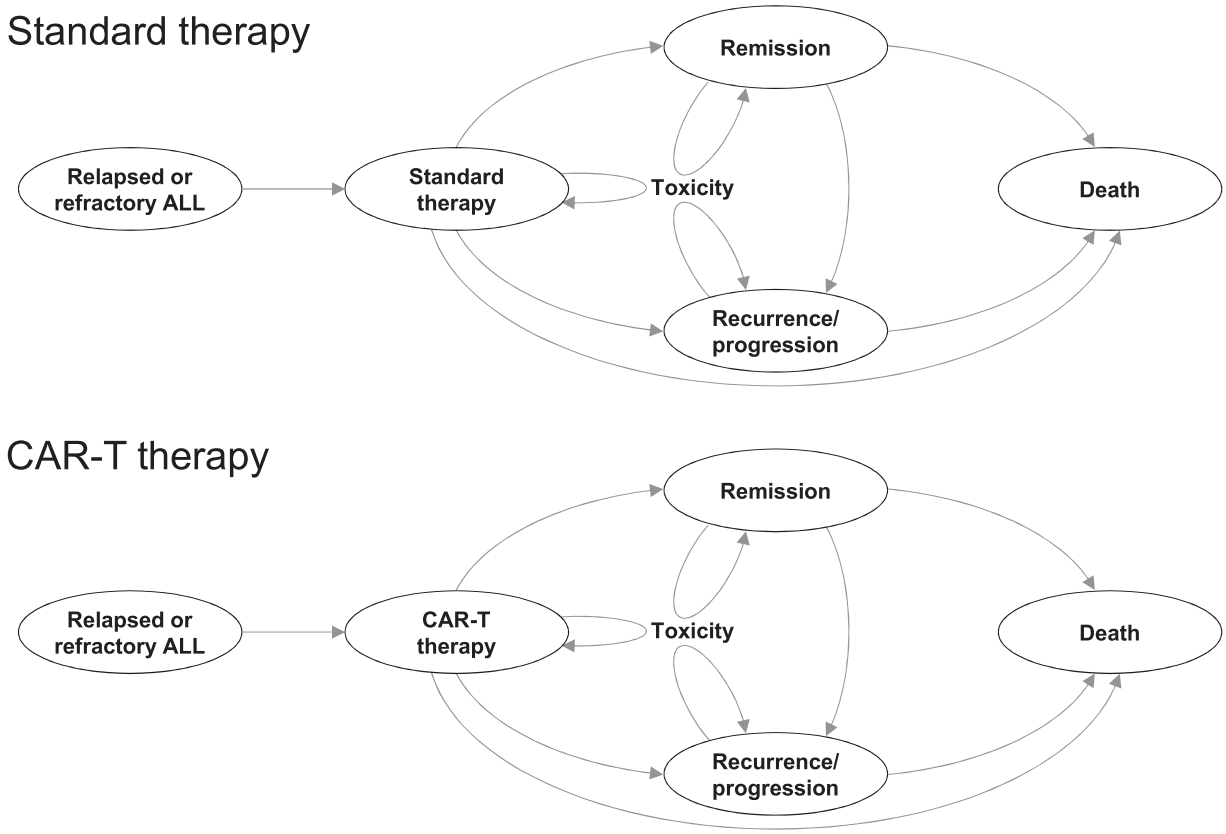


Figure 1. State-transition diagram. This figure demonstrates the primary disease states (**ovals**) of the microsimulation cost-effectiveness model. **Arrows** represent possible transitions from one health state to the next. Patients may experience toxicity and remain in their same state after acquiring a health utility deduction and cost penalty. Patients who initially received CAR-T but experienced disease progression received the standard therapy as salvage. ALL = acute lymphoblastic leukemia; CAR-T = chimeric antigen receptor T cell.

Outcomes Measures

We measured effectiveness in quality-adjusted life-years (QALYs), which represents the product of health utility and survival. Health utility characterizes quality of life, which ranges from 0 (death) to 1 (perfect health). We obtained health utility scores for separate health states from the literature (37–42). For patients experiencing toxicity, we subtracted health utility from their baseline scores. Specific values of health utility and utility reductions and literature sources are provided in Table 1.

Analysis

We conducted this analysis according to principles put forth by the Second Panel on Cost-Effectiveness in Health and Medicine (43). We assumed a third-party payer perspective in our primary base-case analysis, and we also present a secondary analysis according to a societal perspective. The societal perspective includes all costs and utilities associated with an intervention regardless of who incurs them (27,43–45). We simulated health outcomes, costs, and survival over a lifetime horizon with a month-long cycle length, applying a 3% annual discount rate for all costs and QALYs. We evaluated the cost-effectiveness of CAR-T therapy compared to standard of care with an incremental cost-effectiveness ratio (ICER) defined as the incremental cost between the two treatments divided by the incremental effectiveness (incremental QALYs). We used a willingness-to-pay threshold of $100 000/QALY, with ICERs under this benchmark considered cost effective (46). Our base-case microsimulation included 100 000 simulated patients.

We performed one-way deterministic sensitivity analyses on each variable in the model to identify influential parameters. We also conducted a probabilistic sensitivity analysis to determine the impact of uncertainty in all model inputs (transition probabilities, costs, and health utilities) using a Monte Carlo microsimulation with 500 samples and 250 trials. Costs were modeled with gamma distributions; transition probabilities and health utilities were modeled with beta distributions. When not available in the literature, standard deviations for probabilities, costs, and utilities were assumed to be 20% of the mean (27,47). We tested different values of our unknown SDs (range = 10%–40% of the mean), and this did not affect our results (data not shown).

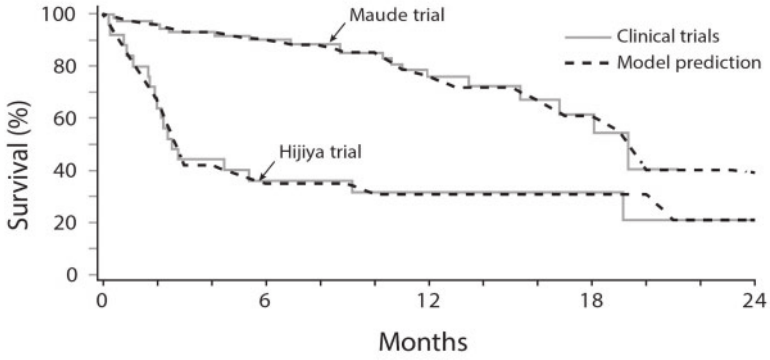
Results

The cost-effectiveness microsimulation model produced progression, survival, and toxicity estimates that closely mimicked the literature (Figure 2 shows model validation results). In our base-case cost-effectiveness analysis, the total cost associated with standard therapy was $440 600, which increased to $968 800 for CAR-T therapy. The effectiveness of standard therapy was 8.58 QALYs, which increased to 16.76 QALYs for CAR-T therapy. CAR-T increased overall cost by $528 200 and improved effectiveness by 8.18 QALYs, which produced an ICER of $64 600 per QALY per payer perspective, which would be considered

Table 1. Parameters for cost-effectiveness model*

Parameter	Value (SD)	Distribution	Reference
Costs			
CAR-T therapy costs			
CAR-T infusion (tisagenlecleucel)	475 000 (95 000)	Gamma	Bach et al., 2017 (12)
Lymphodepleting chemotherapy	1758 (351)	Gamma	AWP (18–23)
ICU admission	32 723 (12 539)	Gamma	Chalom et al., 1999 (32)
Tocilizumab	2048 (410)	Gamma	AWP (18–23)
Infection	4773 (2462)	Gamma	Rashid et al., 2016 (33)
Cytopenia	1655 (331)	Gamma	Ershler et al., 2005; Elting et al., 2003; Michels et al., 2012 (29–31)
Febrile neutropenia	1310 (262)		Michels, et al., 2012 (31)
IVIG	5940 (1188)	Gamma	AWP (18–23)
Standard-of-care costs			
Chemotherapy regimen	51 286 (10 257)	Gamma	AWP (18–23)
Anemia	2134 (427)	Gamma	Ershler et al., 2005 (29)
Thrombocytopenia	1520 (304)	Gamma	Elting et al., 2003 (30)
Febrile neutropenia	1310 (262)	Gamma	Michels et al., 2012 (31)
Infection	4773 (2462)	Gamma	Rashid et al., 2016 (33)
Successful HSCT	299 987 (147 195)	Gamma	Lin et al., 2010 (34)
Failed HSCT	459 682 (355 198)	Gamma	Lin et al., 2010 (34)
General disease-related costs	961 (192)	Gamma	Mariotto et al., 2011 (36)
End-of-life costs	12 867 (17 252)	Gamma	Johnston et al., 2018 (35)
Societal costs†			
Caregiver	577 (115)	Gamma	Li,et al., 2013 (44)
Patient time	1687 (337)	Gamma	Hopkins et al., 2010 (45)
Parking/meals/transportation	315 (63)	Gamma	Tringale et al., 2017 (27)
Health utility			
Baseline ALL	0.94 (0.188)	Beta	Furlong et al., 2012 (38)
Disease progression	−0.64 (0.13)	Beta	Aristides et al., 2015 (40)
Up-front treatment	−0.42 (0.084)	Beta	Hettle et al., 2017 (39)
HSCT	−0.57 (0.114)	Beta	Sung et al., 2003 (37)
Cytokine release syndrome	−0.47 (0.09)	Beta	Beauchemin et al., 2016 (41)
ICU admission	−0.16 (0.03)	Beta	Cuthbertson et al., 2005 (42)
Infection	−0.23 (0.04)	Beta	Beauchemin et al., 2016 (41)
Cytopenia	−0.19 (0.04)	Beta	Beauchemin et al., 2016 (41)
Neurotoxicity	−0.19 (0.04)	Beta	Beauchemin et al., 2016 (41)
Anemia	−0.19 (0.04)	Beta	Beauchemin et al., 2016 (41)
Thrombocytopenia	−0.11 (0.02)	Beta	Beauchemin et al., 2016 (41)
Febrile neutropenia	−0.25 (0.05)	Beta	Beauchemin et al., 2016 (41)
Transition probabilities			
CAR-T transition probabilities			Maude et al., 2018 (11); FDA Drug Advisory Committee Meeting, 2017 (18)
Cytokine release syndrome	0.77 (0.05)	Beta	
ICU admission	0.46 (0.06)	Beta	
Tocilizumab (for cytokine release syndrome)	0.38 (0.06)	Beta	
Infection	0.43 (0.06)	Beta	
Cytopenia	0.37 (0.06)	Beta	
Neurotoxicity	0.4 (0.06)	Beta	
Febrile neutropenia	0.35 (0.06)	Beta	
Complete remission	0.81 (0.05)	Beta	
Overall survival at 1 year	0.76		
Standard-of-care transition probabilities			Hijiya et al., 2011 (17)
Anemia	0.64 (0.1)	Beta	
Thrombocytopenia	0.64 (0.1)	Beta	
Febrile neutropenia	0.6 (0.1)	Beta	
Infection	0.76 (0.09)	Beta	
Complete remission	0.44 (0.1)	Beta	
HSCT after remission	0.91 (0.06)	Beta	
Overall survival at 1 y	0.31		

*Treatment-related, ICU, and end-of-life costs were applied once in 2017 dollars. All other costs are shown as per-month values in 2017 dollars. ALL = acute lymphoblastic leukemia; AWP = average wholesale price; CAR-T = chimeric antigen receptor T cell; HSCT = hematopoietic stem cell transplantation; ICU = intensive care unit; IVIG = intravenous immunoglobulin G.
†Societal costs were included in the societal perspective model only.



Study Outcome	Cost-effectiveness model, %	Literature values, %
Overall Survival (1 year)		
CAR-T	76.1	76.0
Standard of Care	29.9	31.0
Progressive Disease		
CAR-T	19.0	18.7
Standard of Care	59.6	56.0
Major CAR-T Toxicity		
CRS	76.9	77.3
Infection	43.4	42.7
Major SOC Toxicity		
Hematologic	64.1	64.0
Infection	76.0	76.0

Figure 2. Model validation. This figure demonstrates the internal validation of the cost-effectiveness model. The **top panel** (plot) demonstrates how our model (dotted lines) predicts survival compared with the published clinical data from the Maude (11) and Hijiya (17) trials (superimposed). The **bottom panel** (table) demonstrates how our model predicts overall survival, disease progression, and major toxicities compared with the Maude and Hijiya trials. CAR-T = chimeric antigen receptor T cell; CRS = cytokine release syndrome; SOC = standard of care.

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cost effective under the threshold of $100 000 per QALY. When considering a societal perspective, the ICER increased minimally to $69 500 per QALY.

Our cost-effectiveness analysis was most sensitive to assumptions regarding lon- term CAR-T survival, the proportion of CAR-T patients achieving complete remission, and the health utility of posttreatment patients (Figure 3). Our base-case analysis assumed that the 1-year survival of patients receiving CAR-T therapy was 76.0%. If the 1-year survival dropped below 57.8% then the ICER rose above $100 000 per QALY, and CAR-T therapy would not be considered cost effective. When we assumed an optimistic survival model, the ICER of CAR-T therapy decreased to $55 200 per QALY. On the other hand, assuming a pessimistic survival model with an increased risk of long-term mortality, the ICER of CAR-T therapy increased to $101 500 per QALY. Additional sensitivity analyses with survival are included in the Supplementary Table 2 (available online).

Our base-case model assumed an 81.0% complete remission rate based on the Maude trial (11). If this complete remission rate dropped below 56.2%, then the ICER increased above $100 000 per QALY. Our base-case analysis assumed that the long-term health utility of disease-free survivors was 0.94. If this health utility dropped below 0.66, then the ICER rose above $100 000 per QALY. If the cost of CAR T-cell therapy infusion increased from $475 000 to $875 000, then CAR T-cell therapy would become cost-ineffective. Our base model assumed outcome-based pricing where payment was required only for those who respond to CAR-T therapy. If we assumed the cost applied to all patients who receive CAR-T therapy regardless of response, then the ICER would increase to $75 600 per QALY. We assumed that IVIG would be necessary for 18 months in CAR-T therapy responders to treat B-cell aplasia (11), although if B-cell aplasia for long-term responders persisted, and if IVIG was required for more than 15 years, then CAR-T therapy would become cost ineffective. Our base model assumed that CAR-T responders did not require HSCT. If we assume that 10.0% of responders received HSCT the ICER increased to $67 200 per QALY, and if 100% of responders received HSCT the ICER increased to $91 700 per QALY. Our model was not particularly sensitive to assumptions about the risk of toxicity, or other costs or health utilities.

The results of the probabilistic sensitivity analysis are shown in Figure 4. We found that CAR-T therapy would be cost effective 94.8% of the time at a willingness-to-pay threshold of $100 000 per QALY. At a willingness-to-pay threshold of $200 000 per QALY, CAR-T would be cost effective 99.8% of the time.

Discussion

US spending on cancer care rose from $27 billion in 1990 to $87.8 billion in 2014 and is projected to reach $158 billion by 2020 (36,48). The increase in cancer drug prices represents a key component in the uptick of overall cancer expenditure. The average cancer drug price before the year 2000 was under $10 000 per year, although by the year 2012 the cost of 12 of 13 drugs approved for cancer topped $100 000 per year (49). This current

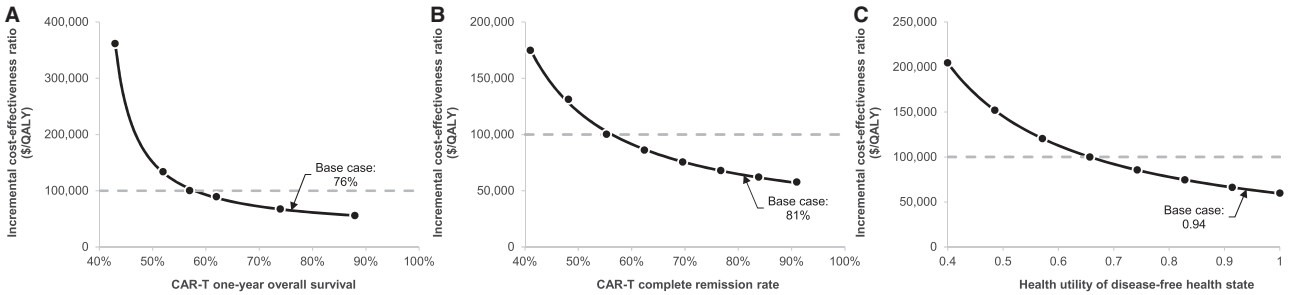

Figure 3. One-way sensitivity analysis. These plots depict the cost-effectiveness of chimeric antigen receptor T-cell (CAR-T) therapy compared to standard therapy as measured with the incremental cost-effectiveness ratio. The **dashed line** reflects the willingness-to-pay threshold of $100 000, with values below this line considered cost effective. Individual plots show how the cost-effectiveness of CAR-T therapy varies by (**A**) CAR-T 1-year overall survival, (**B**) CAR-T complete remission rate, and (**C**) Health utility of disease-free health state. QALY = quality-adjusted life-year.

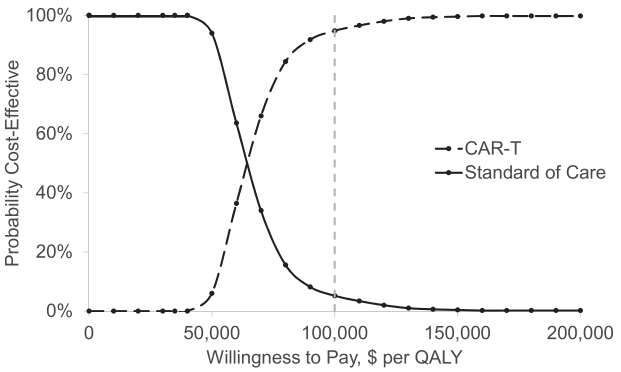

Figure 4. Probabilistic sensitivity analysis. This plot demonstrates a cost-effectiveness acceptability curve. The plot shows the results of a probabilistic sensitivity analysis comparing the cost-effectiveness of chimeric antigen receptor T-cell (CAR-T) therapy with standard therapy for pediatric relapsed/refractory B-cell acute lymphoblastic leukemia. The **gray dotted line** reflects the willingness to pay threshold of $100 000 per quality-adjusted life-year (QALY).

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study evaluated CAR-T therapy, which at $475 000 represents the costliest cancer drug ever approved by the US Food and Drug Administration. Despite the high cost of CAR-T therapy, this study found that the treatment may be cost effective compared to standard therapy—largely due to the substantial survival advantage afforded by CAR-T therapy. This study found that CAR-T therapy led to an improvement of 8 QALYs in pediatric B-ALL patients.

Cost-effectiveness research measures *value* in health care; although value represents an important concept, one must also consider implications of the outright cost and affordability of therapy. These costs affect multiple stakeholders across the health-care spectrum, although the burden of cost increasingly falls on the patient. Recent studies demonstrate that patients increasingly experience the consequences of financial toxicity due to high out-of-pocket costs (49). CAR-T therapy is one of the most expensive treatment options ever introduced to the market, and, if approved by the Food and Drug Administration for multiple indications, could have a dramatic effect on health-care spending and individual patient burden (12). Beyond CAR-T therapy, oncology as a whole represents one of the fastest growing sectors of health-care spending (50), with costly immunotherapy drugs recently becoming first-line standard of care in the management of several common cancers (51,52). The United States spends more on prescription drugs than any country in the industrialized world (53). The $475 000 price of tisagenlecleucel raises the important consideration of "affordability," which stands somewhat apart from "cost-effectiveness." Additionally, these expensive innovative systemic therapies will require equally innovative payment models. This may include the "outcomes-based pay" that Novartis uses for tisagenlecleucel. Other payment options include incremental payments over time rather than fixed up-front sum payment, indication-specific pricing, or models that defer part of the payment until the drug is confirmed to be efficacious with long-term follow-up (54). Health policy involving drug pricing in the United States represents a complex and politically fraught subject—yet meaningful drug policy discourse will become increasingly imperative with the wave of novel costly therapeutics.

Given the high cost of CAR-T therapy other organizations have considered the cost-effectiveness of this class of therapy. The United Kingdom's National Institute for Health and Care Excellence presented a report that found an ICER of £49 994 per QALY, which translates to $US70 014 per QALY (55). Similarly, the Institute for Clinical and Economic Review conducted a cost-effectiveness analysis that found that CAR-T therapy had an ICER of $57 093 per QALY compared to standard therapy (56). Our analysis differs from the above organizations in that we used a microsimulation model rather than a Markov model, permitting more complex model design than traditional Markov models (16). Additionally, we used the recently published results of the ELIANA trial to inform the CAR-T arm of our model (11). Even with the differing techniques and data sources, the ICER in this current study ($64 600 per QALY) was similar to these external reports, which provides external validation to further support the results of this study.

Our cost-effectiveness model's sensitivity to assumptions about survival represents an important point worth discussion. Given the novelty of CAR-T therapy, we lack an understanding about long-term outcomes of patients receiving this therapy. We tested a range of assumptions about the survival benefits of CAR-T therapy and overall found modest sensitivity to assumptions about survival. Despite the findings in our sensitivity analysis, long-term understanding about the efficacy of CAR-T therapy remains unknown, and hypothetical factors such as late relapses or unknown late-developing toxicities could sway cost-effectiveness away from CAR-T therapy.

This cost-effectiveness study has other limitations worth noting. As mentioned, CAR-T therapy is a new therapy and thus we lack long-term data on survival, costs, role of HSCT after CAR-T, and complications that could influence these cost-effectiveness analysis results. Therefore, these early findings of cost-effectiveness for CAR-T therapy could shift with more mature data. Additionally, we lack information on the duration of

long-term B-cell aplasia and the duration of need for costly monthly IVIG. Our sensitivity analyses demonstrate the relative stability of our model under differing circumstances, although unknown future outcomes could sway our study results. Another limitation relates to the quality of data used to inform our model. Ideally cost-effectiveness research would incorporate model inputs from a randomized phase III trial comparing CAR-T therapy to standard of care (57). However, CAR-T therapy has already received approval from the Food and Drug Administration based on the compelling results from phase I/II studies; therefore, because of practical and ethical reasons, it is unlikely we will see a randomized phase III trial in this population. Additionally, producing a batch of CAR-T cells takes time, and a fraction of the patients will not receive their intended CAR-T therapy [18% in the Maude (11) study]. The outcomes of these patients are not well described in the Maude study, and although production speed of CAR-T therapy has increased, incorporating these patients in the model would make CAR-T less cost effective. We assumed that patients who progressed after CAR-T received standard therapy as salvage, increasing cost and decreasing health utility for this patient subset. Given that there is no data on how CAR-T nonresponders will fare with salvage chemotherapy we assumed they had similar response rates as those who did not initially receive CAR-T, which may not be confirmed by longer-term follow-up of CAR-T nonresponders. Lastly, our model inputs including costs and utilities arose from heterogeneous resources, although our cost-effectiveness model was not particularly sensitive to these variables.

Despite these limitations, this study found CAR-T therapy would be considered cost-effective in treating relapsed or refractory pediatric B-ALL patients. However, follow-up to assess long-term outcomes is required to confirm the validity of these preliminary findings.

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Notes

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