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ORIGINAL RESEARCH

Cost-Effectiveness of Brentuximab Vedotin Versus Physician's Choice of Methotrexate or Bexarotene for the Treatment of Cutaneous T-cell Lymphoma in Canada

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ABSTRACT

Introduction: Brentuximab vedotin versus physician's choice of methotrexate (MTX) or bexarotene (BEX) significantly improved progression-free survival (PFS) (median PFS, 16.7 vs. 3.5 months) and delayed time to subsequent treatment (8.4 vs. 3.7 months), with similar overall survival in patients with CD30-expressing mycosis fungoides (MF) or primary cutaneous anaplastic large cell lymphoma (pcALCL), two types of cutaneous T-cell lymphomas.We assessed the cost-effectiveness of brentuximab vedotin versus MTX or BEX from a Canadian healthcare payer perspective in the indicated population.

Methods: A 5-state partitioned survival model [pre-progression, non-stem cell transplant (SCT) post-progression, SCT, SCT relapse, death] with a weekly cycle length and 45-year lifetime horizon has been developed. Health-state occupancies, utility estimates, and treatment duration were informed by ALCANZA. Other inputs and costs came from the literature or clinician experts. Scenario analyses varied key parameters and tested assumptions.

Results: Brentuximab vedotin versus MTX or BEX was cost-effective; the incremental cost-effectiveness ratio was CAN$43,790 per quality-adjusted life year (QALY) gained. Brentuximab vedotin was more effective (incremental life years: 0.15; QALYs: 0.25) and total treatment costs were slightly higher (incremental costs: $11,105) than MTX or BEX. Key model drivers included end-stage care duration, SCT eligibility, and brentuximab vedotin retreatment rates.

Conclusion: Brentuximab vedotin compared with MTX or BEX was cost-effective for CD30-expressing MF and pcALCL. Brentuximab

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vedotin's higher drug costs versus MTX or BEX were offset by decreased post-progression and end-stage management costs, and showed a 0.25 QALY gain versus MTX or BEX, and increased the proportion of patients eligible for potentially curative SCT.

Keywords: Cost-effectiveness; Cutaneous T-cell lymphoma; Economic model

Key Summary Points

Why carry out this study?

Cutaneous T-cell lymphoma (CTCL) is associated with substantial economic burden due to high healthcare resource utilization and costs. Brentuximab vedotin has been approved as a treatment option for CTCL in Canada, specifically for adult patients with primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF), two types of CTCLs, treated previously with systemic therapy.

It is important to analyze the cost-effectiveness of brentuximab vedotin as results from the ALCANZA study show improved, clinically meaningful, durable responses.

We hypothesized that brentuximab vedotin is a cost-effective treatment option for patients with pcALCL or CD30-expressing MF.

What has been learned from the study?

Based on clinical data from the ALCANZA trial and Canadian clinical expert opinion on model inputs, this analysis found that brentuximab vedotin is a cost-effective treatment for CTCL; treatment with brentuximab vedotin compared with MTX or BEX incurred higher drug costs, but most of those costs were offset through reduced costs in the post-progression and end-stage management health states.

Brentuximab vedotin provides a cost-effective treatment option with superior efficacy and a comparable safety profile to physician's choice of MTX or BEX from the perspective of the Canadian publicly funded healthcare system.

INTRODUCTION

Cutaneous T-cell lymphoma (CTCL) is a relatively rare, heterogeneous group of non-Hodgkin lymphomas that present in the skin without evidence of extracutaneous disease at the time of diagnosis [1]. The annual incidence of CTCL is estimated at 11.32 cases per million people in Canada [2]. The most common CTCL subtypes are mycosis fungoides (MF; 60% of CTCLs) and primary cutaneous anaplastic large cell lymphoma (pcALCL); pcALCL is characterized by the expression of cell-surface CD30 antigen [3]. By definition, pcALCL exhibits a high level of CD30 expression (≥ 75% of tumor cells) [4], whereas CD30 expression in MF is more variable [5].

CTCLs often have a chronic disease course and a devastating impact on quality of life, arising from persistent and frequently disabling symptoms, including disfiguring lesions, debilitating pruritus, and frequent skin infections [3, 6]. Advanced stages of CTCL (stages IIB+) can be associated with severe skin tumors, erythroderma, and inferior HRQoL compared with earlier stages of the disease [6]. CTCL is also associated with substantial economic burden due to high healthcare resource utilization and costs [7].

The goals of therapy for CTCL, as indicated by CTCL treatment guidelines, are to improve symptoms, reduce the burden of disease, maintain remission, delay disease progression, and improve or preserve HRQoL [8–12]. Currently, there is no standard therapy for CTCL due to its diverse clinical presentation. Generally, patients with advanced disease are treated with systemic therapies [e.g., oral methotrexate (MTX), bexarotene (BEX), interferon-alpha, targeted therapies, chemotherapy], with the

goal of achieving a response, maintaining adequate organ function, and becoming eligible to receive a potentially curative allogeneic stem cell transplant. For those who are transplant ineligible, the goals are to increase survival, control disease, reduce symptoms, and improve HRQoL [13].

Given the chronic and recurrent nature of the disease, patients may survive for many years with treatment, although they frequently require several types of treatment, repeat treatment courses, and maintenance regimens for ongoing disease and symptom control. These data demonstrate the need for effective treatments that extend duration of response, time in remission, and improve quality of life.

Brentuximab vedotin (Adcetris®; Seagen; Bothell, WA, USA) is a CD30-directed antibody–drug conjugate approved in Canada for six indications, including the treatment of adult patients with pcALCL or CD30-expressing MF treated previously with systemic therapy. The CADTH pan-Canadian Oncology Drug Review Expert Review Committee has recommended the reimbursement of brentuximab vedotin for adult patients with CD30-positive MF or pcALCL previously treated with systemic therapy based on the ALCANZA trial results [14].

ALCANZA was a phase 3 multicenter, open-label, randomized, active controlled trial designed to evaluate the efficacy and safety of brentuximab vedotin ($n = 66$) compared with physician's choice ($n = 65$) of MTX or BEX, in patients with CD30-expressing MF and pcALCL [15]. A clinically meaningful and statistically significant benefit in favor of brentuximab vedotin compared with MTX or BEX was demonstrated in patients achieving an objective response that lasted at least 4 months (ORR4, 56.3% vs. 12.5%, $P < 0.0001$). Brentuximab vedotin compared with MTX or BEX also demonstrated statistically significant improvements in complete response (CR; 16% vs. 2%, $P = 0.0046$), progression-free survival (PFS; 16.7 vs. 3.5 months, $P < 0.0001$), and the Skindex-29 symptom domain [maximum reduction (SD): − 27.96 (26.877) vs. − 8.62 (17.013), $P < 0.0001$].

The objective of this economic evaluation was to estimate the cost-effectiveness of brentuximab vedotin compared with MTX or BEX for the treatment of patients with pcALCL or CD30-expressing MF who have had prior systemic therapy over a lifetime horizon from the perspective of the Canadian publicly funded healthcare system. This analysis is the first cost-effectiveness analysis of brentuximab vedotin in the treatment of CTCL in the Canadian healthcare setting.

METHODS

Patient Population

The target population of this economic evaluation reflects the treatment of adult patients with pcALCL or CD30-expressing MF who have had prior systemic therapy and aligns with the Health Canada-approved indication. The modeled population is consistent with the intent-to-treat (ITT) patient population enrolled in the ALCANZA trial [15]. The control arm in the ALCANZA trial was physician's choice of MTX or BEX, which serves as the base-case model comparator. Although MTX is more commonly used in Canada than BEX, BEX is a relevant comparator as evidenced by its inclusion in the Alberta Health Guidelines and the British Columbia Cancer Benefit Drug List, as well as by its validation by Canadian clinical expert opinion [9, 16, 17].

Model Overview

The model satisfies the standards of health economics required by core health technology assessment authorities, and is aligned with ISPOR Task Force on Good Modeling Practices and CADTH economic guidelines [18, 19]. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

The model was developed in Microsoft Excel® using a partitioned survival analysis in combination with a payoff approach to estimate the proportion of patients in each health state (Fig. 1). Partitioned survival models are

accepted approaches to cost-effectiveness models used to inform health technology assessment submissions of oncology medicines [19, 20]. A payoff approach gives a lump sum of costs and quality-adjusted life years (QALYs) upon reaching a milestone; in this analysis, the milestone is progression. The payoff is continuously discounted, such that it is equivalent to incurring those costs and QALYs over time. The health states modeled were pre-progression (on or off treatment), post-progression (receiving active subsequent therapy, no active subsequent therapy, or receiving end-stage disease management), and death.

Additional health states for patients who receive allogeneic SCT include SCT (disease-free), SCT relapse (receiving active subsequent therapy, no active subsequent therapy, receiving end-stage disease management), or death. The treatment pathways for brentuximab vedotin and either MTX or BEX were the same, although the time spent pre-progression differed between brentuximab vedotin and either MTX or BEX.

All patients enter the model in the pre-progression state, from which most patients will progress to the non-SCT post-progression state, with a small percentage of transplant-eligible patients progressing to SCT, as described in the model inputs. A proportion of patients who respond during pre-progression are eligible to receive allogeneic SCT; these patients may remain disease-free following the procedure or relapse. After progression, patients who did not receive allogeneic SCT undergo multiple lines of active subsequent therapy. Near the end of their lives, patients begin end-stage disease management. Patients who relapse from allogeneic SCT receive the same active subsequent therapy and end-stage care as non-SCT patients, although they do not receive brentuximab vedotin as a subsequent therapy.

The model utilizes a payoff approach when patients reach the post-progression health state, where total post-progression costs and QALYs are determined based on time remaining alive. In each cycle, the proportion of patients leaving the pre-progression state is calculated, and the payoff is applied. Post-progression states include a fixed period spent on active therapy, a period without active therapy, and then the remaining time is spent in end-stage disease management. The difference in payoff between brentuximab vedotin and MTX or BEX in the base case was derived by calculating the area between the overall survival (OS) and PFS curves for non-SCT outcomes, and by calculating the area between the OS and disease-free survival curves for SCT outcomes.

The duration of end-stage management in the base case is 3 months for brentuximab vedotin and 6 months for MTX or BEX, based

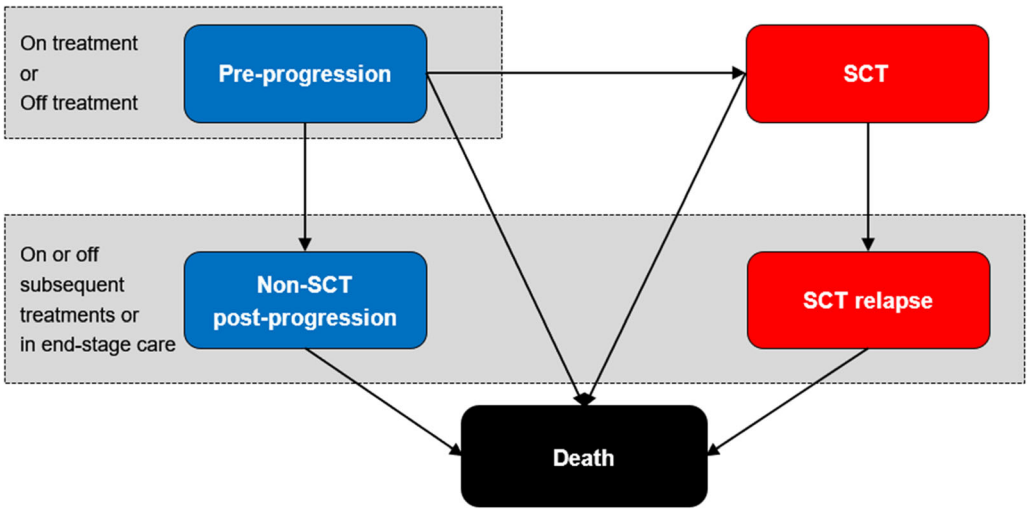

Fig. 1 Model structure diagram. *SCT* stem-cell transplant

Table 1 Model parameters for the base-case analysis

Model specifications	Inputs	
Patients	Previously treated CD30-expressing patients with MF and with pcALCL–ALCANZA ITT population	
Intervention	Brentuximab vedotin	
Comparison(s)	Physician's choice of MTX or BEX, modeled as a single comparator	
Inputs[a]	Costs	Effectiveness
	Drug acquisition and administration	PFS
	Medical resource use	OS
	Adverse event treatment (grade 3 + , > 5%)	Time on treatment
	Subsequent treatments, including SCT	ORR
	End-of-life care	Health-related quality of life
	Clinical	EQ-5D-3L
	Clinician input and validation of model assumptions ($n = 5$)	
Outcomes	Total costs, by category	Cost per LY gained
	Total LYs and QALYs	Cost per QALY gained
	Proportion of patients undergoing SCT	
Perspective	Canadian publicly funded healthcare system	
Timeframe	Lifetime (modeled as 45 years), with flexibility to conduct analyses over shorter time horizons	
Model approach	Partitioned survival model with probabilistic base case	
Discount rate	Costs and QALYs discounted at 1.5% annually	

BEX bexarotene, *ITT* intent to treat, *LY* life year, *MF* mycosis fungoides, *MTX* methotrexate, *ORR* overall response rate, *OS* overall survival, *pcALCL* primary cutaneous anaplastic large cell lymphoma, *PFS* progression-free survival, *QALY* quality-adjusted life year, *SCT* stem cell transplant

[a]See the Supplementary Appendix for additional information on the model inputs

on Canadian clinician opinion [17]. The duration of active subsequent treatment is the same for the brentuximab vedotin and the MTX or BEX arms, as the treatment mix is identical. Time spent off active treatment in the post-progression health state is calculated as the total time in post-progression, less the active subsequent treatment and the end-stage durations for both arms.

The model used a 1-week cycle length, which aligns with the trial dosing schedule and allows for sufficient granularity in transitions between health states. In the base case, a half-cycle correction was applied to all costs other than those for frontline drugs, which are incurred at the start of each cycle.

A time horizon of 45 years was sufficient to capture all lifetime costs and outcomes across the intervention and the comparators [19]. Uncertainty in the time horizon was explored using a range of scenario analyses examining time horizons of 10, 20, and 30 years.

A discount rate of 1.5% annually was applied to both costs and outcomes in the base case, and discount rates of 0% and 3% were used in scenario analyses, as recommended in the most

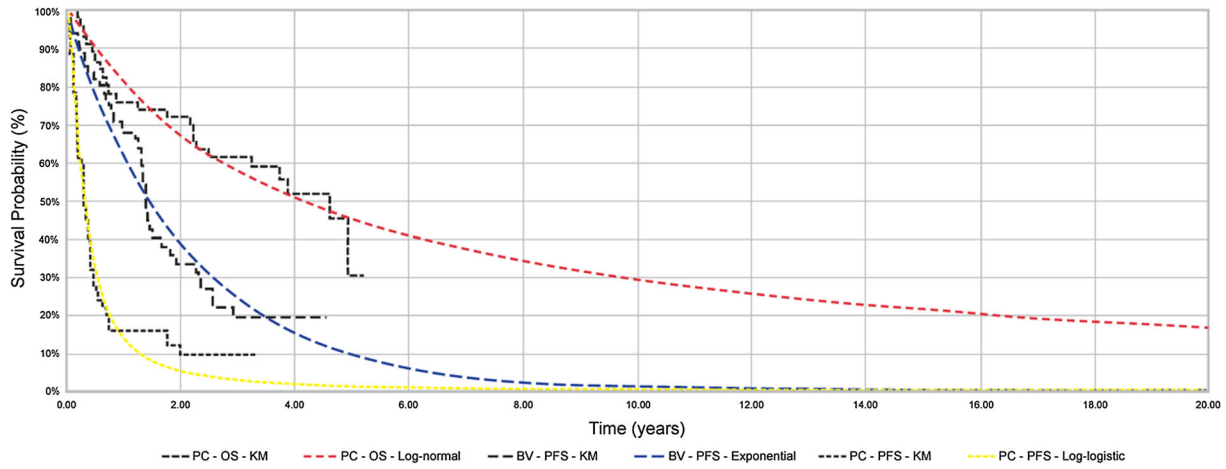

Fig. 2 Kaplan–Meier curves and fitted distributions for OS and PFS in the base-case analysis, ITT population. *BV* brentuximab vedotin, *ITT* intent to treat, *KM* Kaplan-Meier, *OS* overall survival, *PC* physician's choice, *PFS* progression-free survival

Table 2 Discounted base-case results: probabilistic analysis

Treatment	Total			Incremental			Cost per QALY (ICER)
	Costs	QALYs	LYs	Costs	QALYs	LYs	
Brentuximab vedotin	$683,798	6.80	9.18	$11,105	0.25	0.15	$43,790
MTX or BEX	$672,693	6.54	9.03				

BEX bexarotene, *ICER* incremental cost-effectiveness ratio, *LY* life year, *MTX* methotrexate, *QALY* quality-adjusted life year

recent CADTH Guidelines for Economic Evaluation of Health Technologies [19]. In addition, a continuous discounting approach was employed to accurately discount costs and QALYs accrued as a payoff.

The base-case analysis takes the perspective of the Canadian publicly funded healthcare system. Model parameters for the base-case analysis are summarized in Table 1, while inputs and assumptions are described in the following subsections and the Supplemental Appendix. The analysis considered all direct medical costs but not indirect costs.

Model Inputs

Model inputs included efficacy, adverse events, active subsequent therapy, costs, and utilities. Information on these model inputs is provided in the Supplementary Appendix.

In the base case, OS for MTX or BEX was assumed to follow a log-normal distribution. PFS for the ALCANZA ITT population was relatively mature and demonstrated a significant benefit for brentuximab vedotin compared with MTX or BEX. In the base case, an exponential model was chosen for brentuximab vedotin and a log-logistic model for MTX or BEX. The Kaplan–Meier curves and fitted distributions for OS and PFS in the base-case analysis are shown in Fig. 2.

Statistical Analyses

Base-case analyses were conducted using the model specifications noted in Table 1. Probabilistic sensitivity analyses (PSAs) were undertaken to vary inputs simultaneously based upon their assigned distribution to capture the total parameter uncertainty; 10,000 PSA iterations

Table 3 Disaggregated costs, QALY, and LY breakdown (discounted)

	Brentuximab vedotin	MTX or BEX	Incremental (brentuximab vedotin vs. MTX or BEX)
Cost category			
Drug costs	$155,404	$122	$155,283
Admin costs	$1459	$0	$1459
MRU costs	$472,940	$579,907	− $106,967
AE costs	$911	$551	$360
Subsequent costs	$35,830	$86,643	− $50,813
SCT costs	$17,253	$5470	$11,783
Total costs	$683,798	$672,693	$11,105
QALY			
Pre-progression	1.47	0.50	0.97
SCT	0.66	0.21	0.45
Non-SCT PPS active	4.45	5.63	− 1.18
SCT relapse active	0.14	0.04	0.10
Non-SCT palliative care	0.07	0.16	− 0.09
SCT palliative care	0.01	0.00	0.01
Total QALY	6.80	6.54	0.25
LY			
Pre-progression	1.89	0.65	1.24
SCT	0.86	0.27	0.59
Non-SCT PPS active	6.02	7.61	− 1.60
SCT relapse active	0.19	0.06	0.13
Non-SCT palliative care	0.20	0.42	− 0.23
SCT palliative care	0.02	0.01	0.01
Total LY	9.18	9.03	0.15

AE adverse event, *BEX* bexarotene, *LY* life year, *MRU* medical resource use, *MTX* methotrexate, *PPS* post-progression survival, *QALY* quality-adjusted life year, *SCT* stem cell transplant

were run, with results stabilizing at approximately 2000 iterations. Scenario analyses were performed primarily to test structural assumptions made throughout the model. The scenarios tested included changes to discount rates, time horizon, parametric survival model choice, survival assumptions, SCT rate, and end-stage management duration.

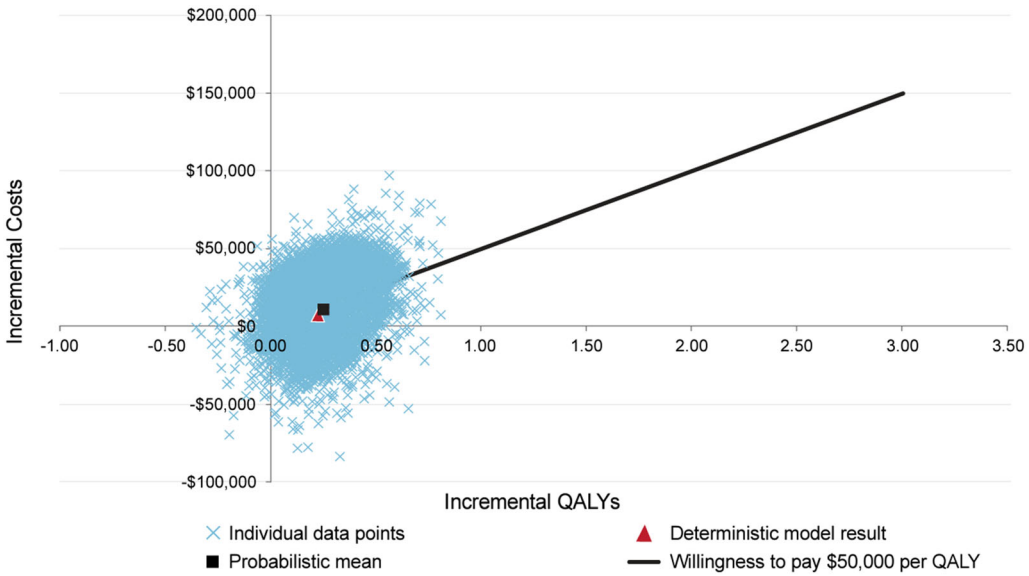

Fig. 3 Cost-effectiveness plane. *QALY* quality-adjusted life year

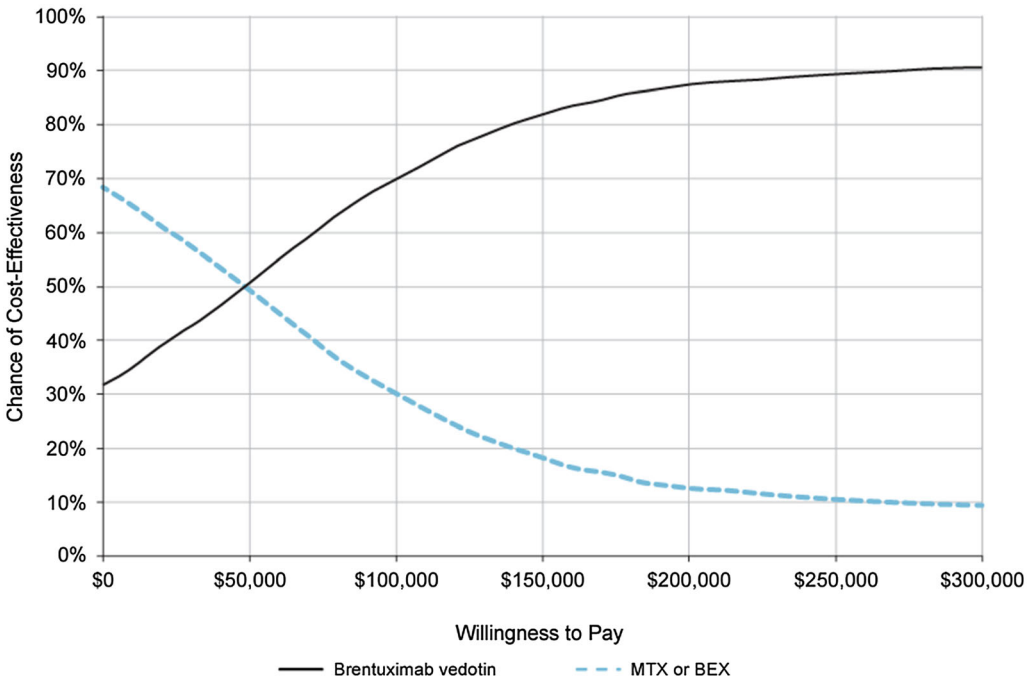

Fig. 4 Cost-effectiveness acceptability curve. *BEX* bexarotene, *MTX* methotrexate

RESULTS

Base-case Probabilistic Analysis

For the base-case probabilistic analysis, brentuximab vedotin yielded greater average LYs and QALYs gained relative to the MTX or BEX treatment arm, mainly driven by improved PFS of brentuximab vedotin compared with MTX or BEX (Table 2). Correspondingly, the total average cost associated with brentuximab vedotin was slightly higher than MTX or BEX, mainly driven by the drug acquisition cost of brentuximab vedotin compared with MTX or BEX. The estimated incremental costs and QALYs accrued by brentuximab vedotin relative to MTX or BEX resulted in an incremental cost-effectiveness ratio (ICER) of $43,790 per QALY gained.

Probabilistic disaggregated costs showed a large upfront cost associated with brentuximab vedotin due to the higher drug costs compared to MTX, in addition to the additional time spent pre-progression and receiving treatment. Brentuximab vedotin SCT costs were also higher due to a higher proportion of brentuximab vedotin patients achieving a CR or PR, and therefore becoming eligible to receive allogeneic SCT. Increased costs due to allogeneic SCT were offset by increased costs in medical resource use in the MTX or BEX arm, again due to the PFS benefit provided by brentuximab vedotin. The savings from the reduced medical resource use also arises from less time spent in the resource-intensive end-stage state, as shown in the disaggregated QALY and LY results (Table 3).

The cost-effectiveness acceptability plane representing 10,000 PSA iterations shows predominately higher incremental QALYs with either lower or higher incremental costs (Fig. 3). The cost-effectiveness acceptability curve shows that, at a willingness-to-pay threshold of $50,000, brentuximab vedotin has a 50.6% chance of being cost-effective and, at a willingness-to-pay threshold of $100,000, a 69.9% chance of being cost-effective (Fig. 4). As the willingness to pay increases, the probability of brentuximab vedotin being cost-effective increases monotonically.

Scenario Analyses

Results from the scenario analyses are shown in Supplemental Table 5. Brentuximab vedotin was more cost-effective in scenarios with lower discount rates, a 10-year time horizon, increased SCT use, and alternative post-progression utility inputs [21].

Scenarios that changed or discounted the end-stage duration led to the largest increase in the ICERs. In two scenarios that assumed the same end-stage duration of 6 and 3 months for brentuximab vedotin and MTX or BEX, ICERs increased to about $286,200 at 6 months and to $283,500 at 3 months, as these scenarios equalize the highly resource-intensive health states.

Substantially increasing the discount rate or shortening the time horizon also reduced the impact of costly post-progression and end-stage care, leading to increased ICERs. In 3 scenarios, the discount rate increased from 0 to 5% and brentuximab vedotin went from dominant to an ICER of nearly $275,000. Similarly, in scenarios where the time horizon increased from 10 to 30 years, brentuximab vedotin went from being dominant to an ICER close to the base-case PSA result. Both of these scenarios reduced, or eliminated, the impact of outcomes further in the future.

DISCUSSION

This cost-effectiveness analysis demonstrated the economic value of brentuximab vedotin compared with MTX or BEX for the treatment of adult patients with pcALCL or CD30-expressing MF who received prior systemic therapy, which aligns with the Health Canada-approved indication. The analysis was based on results for the ITT population from the international, open-label, randomized, phase 3 ALZANCA trial [15]. In the ALCANZA trial, brentuximab vedotin significantly delayed progression, with a median PFS of 16.7 months compared with 3.5 months in the MTX or BEX arm. Delaying progression was important within the economic model, both for maintaining better patient HRQoL for a longer period

(pre-progression utility, 0.77; post-progression utility, 0.61–0.38) and for reducing the amount of time spent in more severe post-progression health states.

A greater proportion of patients in the brentuximab vedotin arm than in the MTX or BEX arm also achieved either a CR or PR, and were therefore potentially eligible to receive allogeneic SCT (brentuximab vedotin, 9.76%; MTX or BEX, 3.10%). Although outcomes for the new Stanford protocol of allogeneic SCT were informed by a single center trial of 53 patients [22], the curative potential of this approach could translate to improved outcomes for eligible patients. Using brentuximab vedotin as the initial therapy for CTCL offers significant value, as an increased response rate means more patients could become eligible to receive potentially curative allogeneic SCT.

The results of this cost-effectiveness analysis were particularly driven by the modeling assumption regarding the OS of brentuximab vedotin compared with that of MTX or BEX. In the base case, OS for brentuximab vedotin and MTX or BEX was assumed to be equivalent. This assumption was supported by clinical expert opinion that an OS benefit was not likely to be observed, as patients often receive several courses of therapy with various agents to provide disease control over the prolonged disease course. In addition, Kaplan–Meier data, as well as results from a parametric survival analysis, showed brentuximab vedotin and MTX or BEX curves crossing, consistent with the assumption that there is no observable difference in OS.

Because a key element of brentuximab vedotin's value is the shorter duration spent in the end-stage management state, it was important to accurately capture the resource use and care required in this state. An end-of-life questionnaire was developed specifically for the model and completed by Canadian providers to collect data to inform resource use in end-stage disease management [23].

Due to the chronic nature of CTCL and the duration of time spent in post-progression health states, the total costs accrued were extremely high. In the case of brentuximab vedotin, cost savings in these health states offset the initial drug costs of brentuximab vedotin and the costs of additional allogeneic SCT procedures. Base-case results were $43,790 per QALY for treatment with brentuximab vedotin compared with MTX or BEX, which falls below the ICERs of other approved therapies for oncology indications in Canada [24]. The model investigated how results were affected by varying key parameters and structural assumptions. Scenario analyses supported the finding that resource use costs during post-progression and end-stage management were a key model driver. Additionally, results from scenario analyses showed that assumptions around end-stage duration and assumptions governing survival extrapolations were the most influential on the cost-effectiveness of brentuximab vedotin. Scenarios assuming equal end-stage duration or substantially discounting post-progression resource use led to the largest ICER increases.

Limitations

This model relied on treatment data obtained from the PROCLIPI Registry and confirmed by expert opinion. Differences in the treatment of CTCL may exist between those used in the real world and those included in this model. For example, although romidepsin can be used for CTCL in Canada, it was not included in the PROCLIPI Registry data and therefore not included in the model. However, analysis of our model results shows that subsequent treatments other than brentuximab vedotin have very little effect on our modeled results. The impact of newer therapies that were not approved at the time of this analysis for CTCL, such as mogamulizumab, is unknown.

While ALCANZA's clinical trial results cannot be generalized to external populations, the use of physician's choice as a comparator was employed to control for this. Furthermore, trial data were supplemented with expert input and external data to inform post-SCT survival and subsequent treatments. However, the level of care and clinical monitoring in clinical trials is often higher than in real-world settings, which likely increased the overall effectiveness of treatment and adverse event recognition, and

may impact the distribution of subsequent treatments.

Patient quality of life is always difficult to measure, and the EQ-5D-3L instrument used to determine utilities may not be fully sensitive to changes in CTCL HRQoL. Comparing the observed utilities from the EQ-5D with those predicted by the Skindex-29 instrument indicates that the EQ-5D lacks sensitivity to this severe condition, and that, by using Skindex-29, the impact on patient HRQoL may be captured to a greater extent [25]. Although the Skindex-29 instrument was shown to be a good predictor of patient HRQoL, the full impact of CTCL on patient HRQoL may not have been captured, and further work is required to determine how best to capture the impact of CTCL on patient quality of life.

Lastly, the model base case was from the perspective of the Canadian publicly funded healthcare system. Although the model offers a comprehensive look at the total cost of treating CTCL, results may not be applicable to other health systems.

CONCLUSIONS

Based on clinical data from the ALCANZA trial and Canadian clinical expert opinion, this analysis found that brentuximab vedotin is a cost-effective treatment for CTCL that significantly improved response rate, delayed disease progression, and allowed a higher proportion of patients to achieve symptom control by reducing disease burden compared with MTX or BEX for the treatment of CTCL. Treatment with brentuximab vedotin compared with MTX or BEX incurred higher drug costs; however, most of those costs were offset through reduced costs in the post-progression and end-stage management health states. Results from sensitivity analyses showed that brentuximab vedotin remained cost-effective when key model parameters were varied under many different structural assumptions. In summary, brentuximab vedotin provides a cost-effective treatment option with superior efficacy and a comparable safety profile to physician's choice of MTX or BEX, from the perspective of the Canadian publicly funded healthcare system.

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Compliance with Ethics Guidelines. The model satisfies the standards of health economics required by core health technology assessment authorities and is aligned with the ISPOR Task Force on Good Modeling Practices and CADTH economic guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors. The authors would like to thank the participants of the ALCANZA study, which provided data for this model.

Data Availability. The datasets analyzed during the current study are available from the corresponding author on reasonable request.

REFERENCES

1. Willemze R, Cerroni L, Kempf W, Berti E, Facchetti F, Swerdlow SH, et al. The 2018 update of the WHO-EORTC classification for primary cutaneous lymphomas. Blood. 2019;133(16):1703–14.

2. Ghazawi FM, Netchiporouk E, Rahme E, Tsang M, Moreau L, Glassman S, et al. Comprehensive analysis of cutaneous T-cell lymphoma (CTCL) incidence and mortality in Canada reveals changing trends and geographic clustering for this malignancy. Cancer. 2017;123(18):3550–67.

3. Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood. 2016;127(20):2375–90.

4. Willemze R, Jaffe ES, Burg G, Cerroni L, Berti E, Swerdlow SH, et al. WHO-EORTC classification for cutaneous lymphomas. Blood. 2005;105(10):3768–85.

5. Edinger JT, Clark BZ, Pucevich BE, Geskin LJ, Swerdlow SH. CD30 expression and proliferative fraction in nontransformed mycosis fungoides. Am J Surg Pathol. 2009;33(12):1860–8.

6. Poligone B, Querfeld C. Management of advanced cutaneous T-cell lymphoma: role of the dermatologist in the multidisciplinary team. Br J Dermatol. 2015;173(4):1081–3.

7. Tsang Y, Gu T, Sharma G, Raspa S, Drake B 3rd, Tan H. Healthcare resource utilization, costs of care, and treatment of mycosis fungoides cutaneous T-cell lymphoma patterns in a large managed care population: a retrospective US claims-based analysis. J Dermatolog Treat. 2018;29(8):747–53.

8. Wilcox RA. Cutaneous T-cell lymphoma: 2016 update on diagnosis, risk-stratification, and management. Am J Hematol. 2016;91(1):151–65.

9. Alberta Health Services. Clinical Practice Guideline LYHE-002 Version 12 2019 [updated September. Available from: https://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-lyhe002-lymphoma.pdf.

10. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas (Version 2.2021) 2021

[updated Mar 4. Available from: https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf.

11. Willemze R, Hodak E, Zinzani PL, Specht L, Ladetto M, Committee EG. Primary cutaneous lymphomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2018;29(Suppl 4):iv30–40.

12. Trautinger F, Eder J, Assaf C, Bagot M, Cozzio A, Dummer R, et al. European Organisation for Research and Treatment of Cancer consensus recommendations for the treatment of mycosis fungoides/Sézary syndrome - Update 2017. Eur J Cancer. 2017;77:57–74.

13. Canadian Agency for Drugs and Technologies in Health (CADTH) Pan-Canadian Oncology Drug Review (pCODR) final clinical guidance report: brentuximab vedotin (Adcetris). 2020; https://www.cadth.ca/sites/default/files/pcodr/Reviews2020/10213BrentuximabVedotinpcALCLMF_fnCGR_NOREDACT_Post03Dec2020_final.pdf.

14. Pan-Canadian Oncology Drug Review. Initial recommendation for brentuximab vedotin (Adcetris) for primary cutaneous anaplastic large cell lymphoma mycosis fungoides. 2020 [Available from: https://www.cadth.ca/sites/default/files/pcodr/Reviews2020/10213BrentuximabVedotinpcALCLMF_inRec_01Oct2020_Post_final.pdf.

15. Prince HM, Kim YH, Horwitz SM, Dummer R, Scarisbrick J, Quaglino P, et al. Brentuximab vedotin or physician's choice in CD30-positive cutaneous T-cell lymphoma (ALCANZA): an international, open-label, randomised, phase 3, multicentre trial. Lancet. 2017;390(10094):555–66.

16. BC Cancer. BC Cancer Benefit Drug List 2020 [updated February 2020. Available from: http://www.bccancer.bc.ca/systemic-therapy-site/Documents/Policy%20and%20Forms/Benefit%20Drug%20List.pdf.

17. BresMed. Brentuximab vedotin CTCL KOL feedback. 2019.

18. Caro JJ, Briggs AH, Siebert U, Kuntz KM. Modeling good research practices–overview: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force–1. Value Health. 2012;15(6):796–803.

19. Lee KM, McCarron CE, Bryan S, Coyle D, Krahn M, McCabe C. Guidelines for the Economic Evaluation of Health Technologies: Canada — 4th Edition 2017 [updated Mar. Available from: https://www.cadth.ca/dv/guidelines-economic-evaluation-health-technologies-canada-4th-edition.

20. Latimer N. NICE DSU Technical Support Document 14: Survival Analysis for Economic Evaluations Alongside Clinical Trials - Extrapolation with Patient Level Data 2011 [updated Mar 2013. Available from: http://nicedsu.org.uk/technical-support-documents/survival-analysis-tsd/.

21. Swinburn P, Shingler S, Acaster S, Lloyd A, Bonthapally V. Health utilities in relation to treatment response and adverse events in relapsed/refractory Hodgkin lymphoma and systemic anaplastic large cell lymphoma. Leuk Lymphoma. 2015;56(6):1839–45.

22. Morris S. Reduced intensity allogeneic stem cell transplantation for advanced stage mycosis fungoides and Sézary syndrome. A Series of 53 patients from the UK. Eur J Cancer. 2018;101:S36.

23. PDCI Market Access. End of Life Clinical Questionnaire. 2020.

24. Chabot I, Rocchi A. How do cost-effectiveness analyses inform reimbursement decisions for oncology medicines in Canada? The example of sunitinib for first-line treatment of metastatic renal cell carcinoma. Value Health. 2010;13(6):837–45.

25. Dummer R, Prince HM, Whittaker S, Horwitz SM, Kim YH, Scarisbrick J, et al. Patient-reported quality of life in patients with relapsed/refractory cutaneous T-cell lymphoma: results from the randomised phase III ALCANZA study. Eur J Cancer. 2020;133:120–30.