Cost-effectiveness of Blinatumomab Versus Standard of Care in Adult Patients With Philadelphia Chromosome-Positive Relapsed or Refractory B-cell Precursor Acute Lymphoblastic Leukemia From a Canadian Healthcare Sector Perspective

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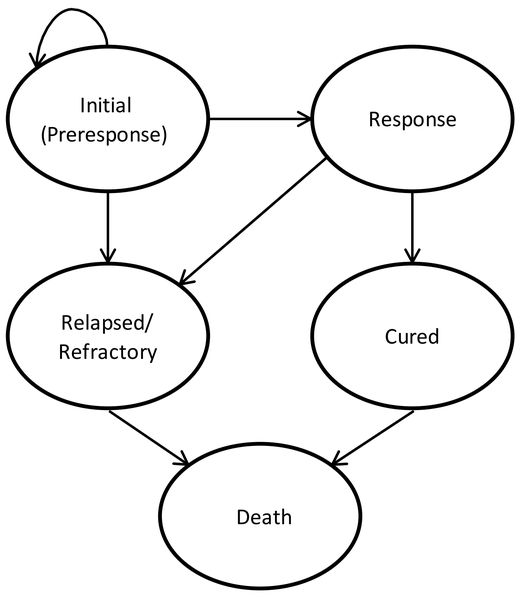
OBJECTIVE

- To evaluate the cost-effectiveness of blinatumomab vs standard of care (SOC) therapy in patients with Philadelphia chromosome-positive (Ph+) relapsed or refractory (R/R) B-cell precursor acute lymphoblastic leukemia (BCP-ALL) from a Canadian publicly funded healthcare payer perspective.

METHODS

- A partitioned survival model (PSM) was developed to estimate the incremental cost-effectiveness ratio (ICER) of blinatumomab vs SOC.
- Where available, PSM estimates were informed by the ALCANTARA study and a historical comparator (HC) study.
- The HC population was matched to patients in ALCANTARA using inverse probability of treatment weights (IPTW) based on average treatment effects on the treated (ATT) weights.
- Parametric distributions were fit to individual patient data from the studies to estimate relapse-free and overall survival.
- Because of the small size population, RFS in the HC study could not be projected. Therefore, only RFS data from ALCANTARA was used to project the time patients spent in the response state for both the blinatumomab and SOC arms.
- Selection of parametric distributions for OS and RFS were based on several factors, including internal consistency, statistical fit, visual fit, and evidence related to the underlying treatment effect model.
  - RFS: RCS log-normal distribution was selected based on Bayesian Information Criterion (BIC) and good visual fit
  - OS: RCS log-logistic distribution was selected based on BIC and good visual fit

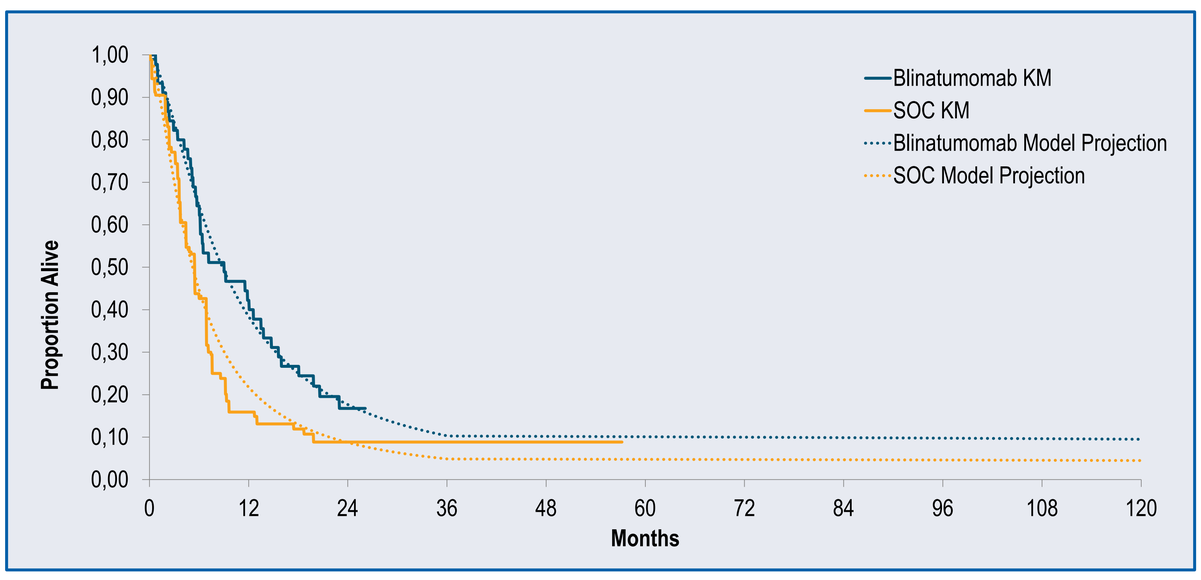
Figure 1. Partitioned Survival Model Schematic



Partitioned Survival Model Structure

- The partition survival model included 5 health states: initial (pre-response), response, R/R, cured, and death.
- All patients started in the initial (pre-response) for up to 12 weeks (unless death occurred) at which point response was evaluated and moved to either the response or R/R state.
- Patients who responded were at risk of relapse for the first 3 years of treatment.
- The model assumed that patients surviving for 3 years would be cured and no longer be at risk of ALL-related mortality.
  - Patients were then assumed to have a twofold excess relative to background mortality

Figure 2. Observed and Predicted Overall Survival



Key Model Inputs and Data Sources

- Patients receiving SOC were assumed to receive a mix of TKIs and chemotherapy (ponatinib and/or hyper-CVAD) consistent with the distribution of treatments observed in the historical comparator study.
- Clinical inputs to inform health-state probabilities for blinatumomab and SOC therapy ~~(ponatinib and/or hyper-CVAD)~~ were based on data from the propensity score analysis of ALCANTARA and the HC study
  - Blinatumomab response rate: 35.6%
  - SOC response rate: 20.9%
- Since utility data were not available in ALCANTARA, utilities were informed using EQ-5D data from the TOWER study (ie, patients with R/R Ph- BCP-ALL).
  - A Delphi panel survey of 17 hemato-oncologists in Europe suggested that baseline utility in adult R/R BCP-ALL would be broadly similar irrespective of Ph status.[1]
- Cost estimates were obtained from published sources.
- A lifetime (30-year) time horizon was used.

Table 2. Utility Values Used in the Model

Health State	Value
Blinatumomab	
Initial	0.740
Response	0.779
Relapsed/refractory	0.686
Standard of care	
Initial	0.671
Response	0.731
R/R	0.686
Terminal decrement	0.033

METHODS (Continued)

Table 3. Costs Used in the Model

Parameter	Point Estimate	Source
Medication costs		
Blinatumomab cost per 38.5 mcg vial (CAD)	2,978	
Blinatumomab dose per day of treatment, week 1 (mcg)	9	Blincyto product monograph
Blinatumomab dose per day of treatment, week 2+ (mcg)	28	Blincyto product monograph
Chemotherapy cost per course (CAD)	116,282	Association Québecoise des Pharmaciens Propriétaires. Liste de Médicaments de L'AQPP. 2018[2] Ontario Case Costing Initiative (OCCI) Code C910 for ALL[3]
TKI monotherapy cost per course (CAD)	55,689	Pan-Canadian Oncology Drug Review (pCODR) Expert Review Committee (pERC) Final Recommendation[4]
Chemotherapy + TKI	171,971	
Administration costs		
Blinatumomab: inpatient days per cycle received (cost per 42-day cycle)		
Cycle 1	9	Blincyto product monograph
Cycle 2	2	Blincyto product monograph
Cycles 3–4	0	Blincyto product monograph
Cost per inpatient day (CAD)	2,234	Average inpatient cost for OCCI Code C910 for ALL[3]
Blinatumomab: outpatient care		
Days per bag change	3.5	Assumption
Cost per day of home infusion therapy (CAD)	4.14	Vereburn Medical Supply. 2017[5]
Cost per bag change (CAD)	37	Statistics Canada National Occupational Classification data
IT CNS prophylaxis	58.32	Ontario Drug Benefit Formulary/Comparative Drug Index. 2017.[6] Ontario Schedule of Benefits (Code G381).[7]
Cost of HSCT (CAD)	124,827	OCCI data (Code C910, CMG 610 – bone marrow/stem cell transplant, inflated to reflect 2018 value)[3]
Cost per course of subsequent salvage therapy (CAD)	116,282	Equal to cost of hyper-CVAD course
Cost of terminal care (CAD)	9,562	OCCI (CMG 810, palliative care for acute patients) and applied as one-time costs to patients who died[3]

CNS central nervous system, HSCT hematopoietic stem cell transplant, IT intrathecal, SOC standard of care, TKI tyrosine kinase inhibitor

RESULTS

- Probabilistic results were based on 5,000 simulations.
- The model estimated a 1.24 life-year gain and 1.00 additional quality-adjusted life years (QALYs) for patients treated with blinatumomab vs SOC.
- While mean blinatumomab related medication costs were CAD 127,543 higher than those for SOC therapy, they were partially offset by lower incremental administration (CAD –51,070), transplant (CAD –4,162), and post-relapse (CAD –4,331) costs.
- The mean probabilistic ICER for blinatumomab vs SOC was CAD 68,185/QALY, and blinatumomab was cost-effective in 70% of simulations at an ICER threshold of CAD 100,000/QALY.
- Extensive scenario analyses were conducted. Along with the cure assumptions, key drivers for ICER were the duration of blinatumomab therapy and model time horizon.

Table 4. Results of the Probabilistic Cost-Effectiveness Analysis

	Blinatumomab	SOC	Blinatumomab vs SOC
Effectiveness, discounted			
Initial	0.22	0.21	0.01
Response	0.33	0.19	0.14
Relapsed/refractory	0.52	0.33	0.19
Cured	1.73	0.83	0.90
Total life years	2.79	1.56	1.24
Total QALYs	2.15	1.15	1.00
Costs, discounted (CAD)			
Medication and administration	184,389	107,915	76,474
HSCT	26,534	30,695	–4,162
Post-relapse	108,919	112,715	–3,796
Terminal care	8,522	9,057	–535
Total	328,364	260,382	67,981
Cost-effectiveness			
Cost per QALY (CAD/QALY)			68,185

HSCT hematopoietic stem cell transplant, QALY quality adjusted life year, SOC standard of care

DISCUSSION

- PSM is a transparent, intuitive approach which yields estimates of survival that correspond closely to survival observed during the study that are the basis for the evaluation.
- However, the PSM approach does not permit explicit modelling of dependencies among clinical events such as response, relapse, HSCT, receipt of salvage therapy, and survival.
- Given the relative importance of OS in determining the economic value of blinatumomab in this indication, and availability of long-term survival for patients receiving SOC from the HC study (up to approximately 8 years), the strength of the PSM in fitting to observed survival outweighs the benefit of a more complex structural model of OS based on interim endpoints.
- Assuming a willingness to pay threshold of CAD $100, 000, the probability of blinatumomab being cost-effective was 69.9%.
- 17 probabilistic scenario analyses results were explored. Most scenarios (15/17) demonstrated that changing parameters had a limited impact on the results (i.e., ICER < CAD $100, 000). The model was most sensitive to changes to the time horizon and cure assumptions.

CONCLUSIONS

- Adult R/R Ph+ BCP-ALL is associated with a poor prognosis and substantial disease burden. There is a clear unmet need for alternatives to TKIs because patients commonly develop resistance to their effects and outcomes remain poor.
- **Compared with SOC, blinatumomab is a cost-effective treatment option for adults with Ph+ R/R BCP-ALL from a Canadian healthcare perspective.**
- **Blinatumomab provides a valuable alternative to systemic agents, as demonstrated by improvements in survival and quality of life.**

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DISCLOSURE

- The study was funded by Amgen.