Curr Oncol, Vol. 21, pp. e541-550; doi: http://dx.doi.org/10.3747/co.21.1837

ORIGINAL ARTICLE

Cost-effectiveness of first-line treatments for patients with *KRAS* wild-type metastatic colorectal cancer

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ABSTRACT

Background

Combinations of chemotherapy regimens and monoclonal antibodies have been demonstrated to improve clinical outcomes in patients with metastatic colorectal cancer (mCRC). Although these combination treatment strategies are safe and effective in first-line treatment for mCRC, little is known about their economic consequences and resource allocation implications. In the present study, we evaluated the cost-effectiveness of bevacizumab plus FOLFIRI, cetuximab plus FOLFIRI, and panitumumab plus FOLFIRI for patients with *KRAS* wild-type mCRC.

Methods

A Markov model simulated the lifetime patient outcomes and costs of each first-line treatment strategy and subsequent lines of treatment from the perspective of the health care payer in Ontario. The model was parameterized using data from the Ontario Cancer Registry, Ontario health administrative databases, and published randomized control trials. Patient outcomes were measured in quality-adjusted life years (QALYS), and costs were measured in monetary terms. Costs and outcomes were both discounted at 5% and expressed in 2012 Canadian dollars.

Results

For mCRC patients with *KRAS* wild-type disease, the treatment strategy of bevacizumab plus FOLFIRI was found to dominate the other two first-line treatment strategies. Sensitivity analyses revealed that the incremental cost-effectiveness ratio values were sensitive to the effectiveness of treatment, the costs of bevacizumab and cetuximab, and health utility values.

Conclusions

Evidence from Ontario showed that bevacizumab plus FOLFIRI is the cost-effective first-line treatment strategy for patients with *KRAS* wild-type mCRC. The panitumumab plus FOLFIRI and cetuximab plus FOLFIRI options were both dominated, but the cetuximab plus FOLFIRI strategy must be further investigated given that, in the sensitivity analyses, the cost-effectiveness of that strategy was found to be superior to that of bevacizumab plus FOLFIRI under certain ranges of parameter values.

KEY WORDS

Cost-effectiveness, metastatic colorectal cancer, wild-type *KRAS,* bevacizumab, cetuximab, panitumumab, FOLFIRI, Ontario

1. INTRODUCTION

In 2008, colorectal cancer affected more than 1.24 million people and caused 608,700 deaths worldwide[1]. In Canada, colorectal cancer is the 2nd most common cause of cancer death: in 2012 approximately 23,300 new cases were diagnosed, and an estimated 9200 deaths were attributed to colorectal cancer[2]. Of patients diagnosed with colorectal cancer, approximately 15%–25% will present with metastatic disease, and 40%–50% will eventually develop metastases[3].

Since the early 2000s, several new treatment options have been developed for metastatic colorectal cancer (mCRC), and various chemotherapeutic regimens and targeted monoclonal antibodies such as bevacizumab, cetuximab, and panitumumab have been widely adopted into clinical practice. Two chemotherapy regimens, FOLFOX (oxaliplatin, 5-fluorouracil, leucovorin) and FOLFIRI (irinotecan, 5-fluorouracil, leucovorin), are considered by many clinicians to be the first-line treatment options for patients with mCRC. Although the two regimens are similar in terms of overall response rate, time to progression, progression-free survival (PFS), and

overall survival (OS)[4,5], they differ in terms of toxicity profile. In particular, patients receiving FOLFOX often experience neurotoxicity, and patients receiving FOLFIRI experience gastrointestinal side effects[4,5]. Use of these chemotherapy regimens alone generally leads to an OS duration of less than 20 months[6,7].

Bevacizumab combined with FOLFIRI or FOLFOX as a first-line treatment choice for mCRC has been investigated in a number of randomized clinical trials (RCTs). Bevacizumab is a humanized monoclonal antibody that targets vascular endothelial growth factor A, a key mediator in cancer cell angiogenesis[8]. Several clinical trials demonstrated that, compared with FOLFIRI or FOLFOX alone[7,9], combination therapy led to an increase in overall response rate and PFS, and an OS duration of more than 20 months[10,11]. A meta-analysis of published clinical trials confirmed a survival advantage for the addition of bevacizumab to chemotherapy in mCRC[12]. Those promising results led, in 2005, to the approval by Health Canada[13,14] and the U.S. Food and Drug Administration[15,16] of bevacizumab in combination with fluoropyrimidine-containing chemotherapy regimens in the first-line treatment of patients with mCRC. Since 2008, bevacizumab plus FOLFIRI has been publically funded as the first-line treatment for patients with mCRC in Ontario[14].

In recent years, two other monoclonal antibodies, cetuximab and panitumumab, have also been investigated as potential treatment options for patients with mCRC. Cetuximab and panitumumab are both immunoglobulin G monoclonal antibodies that target the epidermal growth factor receptor. Both treatments have been shown to be effective in patients with a wild-type *KRAS* (*KRAS* WT) gene; mutated *KRAS* acts as a predictive biomarker of resistance to treatment with cetuximab and panitumumab[17,18]. Several clinical studies have shown that, compared with FOLFIRI or FOLFOX alone, the combination of cetuximab or panitumumab with FOLFIRI or FOLFOX led to improvements in overall response rate, PFS, and OS in *KRAS* WT patients[10,19,20]. The cost-effectiveness of these three first-line treatment strategies—bevacizumab plus FOLFIRI, cetuximab plus FOLFIRI, and panitumumab plus FOLFIRI—for mCRC patients with *KRAS* WT has not previously been investigated. We investigated the cost-effectiveness of these three treatment strategies from the perspective of the Ontario health care payer.

2. METHODS

2.1 Data Sources

To date, no RCT has produced effectiveness data for the three treatment strategies under consideration. Thus, our model was parameterized using effectiveness data from Ontario health administrative data and relevant efficacy data from phase III and IV RCTs.

Through the Cancer Data Linkage project, we obtained, from administrative databases in the province of Ontario, individual-level data for all patients diagnosed with colorectal cancer. From those data, we identified patients diagnosed with mCRC who received bevacizumab plus FOLFIRI as first-line treatment between January 1, 2008, and December 31, 2009. During that period, the Ministry of Health and Long-Term Care (MOHLTC) in Ontario reimbursed bevacizumab only in combination with FOLFIRI, making that combination the most commonly prescribed regimen in the province. Figure 1 describes the selection of the patient cohort for the study.

Estimates of treatment efficacy (OS and PFS) in patients receiving first-line cetuximab plus FOLFIRI[10,19], panitumumab plus FOLFIRI[20], second-line FOLFOX and FOLFIRI[4], third-line panitumumab[21], and best supportive care[21] were taken from published phase III and IV RCTs. Ethics approval was obtained from Western University's Ethics Board. Table I shows patient characteristics for the study cohort.

2.2 Model Overview

We developed a decision analytic model to simulate the lifetime clinical and economic consequences associated with mCRC patients, capturing initiation of first-line treatment, subsequent lines of treatment, and eventual death. Table II shows the parameter estimates.

The model had three separate arms representing each of the possible combination-treatment strategies [Figure 2(A)]. At the end of each arm, a Markov model captured all the possible health states, including death, for the patients over time. Model M1 represented treatment consisting of bevacizumab plus FOLFIRI and had six health states [Figure 2(B)]:

- First-line treatment with bevacizumab plus FOLFIRI
- Cancer-free state
- Second-line treatment with FOLFOX
- Third-line treatment with panitumumab monotherapy

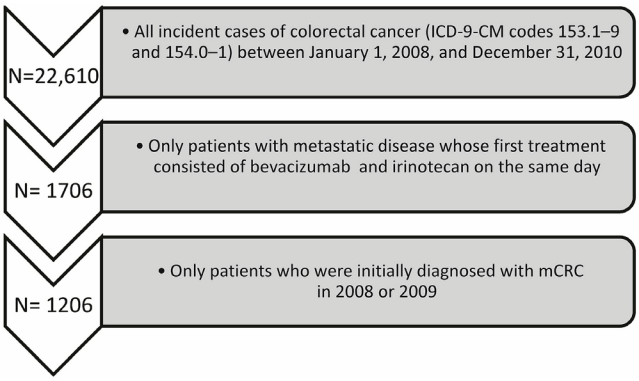

FIGURE 1 Selection of the patient cohort. ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification; mCRC = metastatic colorectal cancer..

- Best supportive care
- Death

Model M1 represents the treatment strategy used in current clinical practice for patients in Ontario. Models M2 and M3 represent treatment scenarios associated with cetuximab plus FOLFIRI and panitumumab plus FOLFIRI respectively [Figure 2(C,D)]. The treatment pathways described in the models are consistent with the scenarios most likely encountered for patients with mCRC in Ontario (based on the expert opinion of one author). Each Markov model was run for a time horizon of 100 months to capture the entire expected lifetime outcome for the cohort. The model was constructed using TreeAge Pro Suite 2009 (TreeAge Software, One Bank Street, Williamstown, MA, U.S.A.).

TABLE I Patient characteristics, Ontario data

Characteristic	*Value*
Patients (*n*)	1216
Diagnosis year (%)	
2008	50.40
2009	49.60
Sex (%)	
Women	39.94
Men	60.06
Age category (%)	
<50 Years	15.61
50–54 Years	13.18
55–59 Years	15.32
60–64 Years	18.21
65–69 Years	14.96
70–74 Years	14.57
75+ Years	8.14
Site of primary tumour (%)	
Colon	63.08
Rectum	27.22
Other	9.7
Metastatic sites (%)	
1	79.40
>1	20.60
Height (cm)	169.0±11.9
Weight (kg)	74.8±16.8
Drugs received (%)	
Bevacizumab	100
Irinotecan	100
Oxaliplatin	38.1
Panitumumab	8.4
Cetuximab	5.6

2.3 Transition Probabilities

We used Kaplan–Meier PFS and OS survival estimates from the Ontario administrative data and from published clinical trial data to estimate monthly state-dependent transition probabilities. Following the approach suggested by Fleurence and Hollenbeak[22] and Ishak *et al.*[23], we fit Weibull distributions to each Kaplan–Meier survival curve to extrapolate survival beyond the time horizon of each trial. The monthly transition probabilities were then determined from the shape (Γ) and scale (λ) parameters of the resultant Weibull distributions. Transition probabilities for a cycle of 1 month were derived using the formula

$$(\text{transition probability})_t = 1 - \text{EXP}\{\lambda[t^{\Gamma} - (t+1)^{\Gamma}]\},$$

where EXP is the exponent function, and t is time.

In all models, mortality unrelated to cancer progression was obtained from Statistics Canada's published life-tables for age-dependent background mortality[24].

2.4 Health Utilities and Costs

Health utilities for each health state, based on the EQ-5D health questionnaire, were obtained from a review of the published literature (Table II). Direct medical costs were estimated from the OHIP (Ontario Health Insurance Plan), Ontario Drug Benefit, National Ambulatory Care Reporting System, Canadian Institute for Health Information Discharge Abstract, and Home Care databases. For each patient in the cohort, we calculated all direct medical costs for 2 years. We then used that information to estimate the monthly state-dependent cost. The direct medical costs include the costs of *KRAS* testing, cancer clinic visits, outpatient physician services, laboratory and other health services, hospitalizations and emergency department visits, drug costs accrued by patients 65 years of age and older, and home care services. Monthly treatment costs were obtained as cost per milligram administered using cost data from the MOHLTC's New Drug Funding Program database. The average cost per month was then determined using the average height and weight of patients in the cohort and the assumption that a patient would receive 2 treatment cycles monthly until disease progression. The costs per milligram for cetuximab and for panitumumab were also determined through the New Drug Funding Program database because both drugs are publicly funded for later treatment lines in mCRC patients in Ontario.

The costs associated with the treatment of grades 3 and 4 adverse events were determined from OHIP fee codes, a literature review, and consultation with a medical oncologist and hospital formulary. The monthly cost of treating each adverse event

TABLE II Model parameters

Variable	*Base-case value*	*Duration*	*Ranges tested in sensitivity*	*Probability distribution*	*Reference*
Treatment costs					
Bevacizumab	$3,758	Treatment course	±20%	Lognormal (8.01, 0.67)	Ontario New Drug Funding Program (NDFP)
Cetuximab					
Initial dose	$4,880	Treatment course	±20%	Lognormal (8.27,0.67)	NDFP
Subsequent doses	$3,240	Treatment course	±20%	Lognormal (7.86,0.67)	NDFP
Panitumumab	$5,394	Treatment course	±20%	Lognormal (8.37,0.67)	NDFP
FOLFIRI	$440	Treatment course	±20%	Lognormal (5.86,0.67)	NDFP, London Health Sciences Centre (LHSC)
FOLFOX	$3230	Treatment course	±20%	Lognormal (7.86, 0.67)	NDFP, LHSC
Infusion time	$426	Treatment course	±20%	Lognormal (5.83,0.47)	LHSC
Pharmacy preparation	$94	Treatment course	±20%	Lognormal (4.32,0.48)	LHSC
Total first-line costs	Varying by month	Treatment course	±20%	Lognormal (varying by month)	OHIP, Ontario Drug Benefit (ODB) Program, Home Care Database (HCD), National Ambulatory Care Reporting System (NACRS), CIHI Discharge Abstract Database (DAD)
Cancer-free costs	$359.40	First 48 months	±20%	Lognormal (5.66, 0.67)	CIHI
	$543.15	Subsequent months	±20%	Lognormal (6.07, 0.67)	CIHI
Total second-line costs	Varying by month	Treatment course	±20%	Lognormal (varying by month)	OHIP, ODB, HCD, NACRS, DAD
Total third-line costs	Varying by month	Treatment course	±20%	Lognormal (varying by month)	OHIP, ODB, HCD, NACRS, DAD
Total best supportive care costs	Varying by month	Treatment course	±20%	Lognormal (varying by month)	OHIP, ODB, HCD, NACRS, DAD
Adverse event costs					
Bevacizumab plus FOLFIRI	$2.24	Treatment course	±20%	Lognormal (0.22, 0.76)	Ramsey *et al.*, 2000[25]
Cetuximab plus FOLFIRI	$53.87	Treatment course	±20%	Lognormal (3.81, 0.42)	Van Cutsem *et al.*, 2009[10]
Panitumumab plus FOLFIRI	$155.27	Treatment course	±20%	Lognormal (4.82, 0.47)	Douillard *et al.*, 2010[20]
FOLFOX	$4.86	Treatment course	±20%	Lognormal (1.32, 0.59)	Colucci *et al.*, 2005[4]
FOLFOX plus bevacizumab	$4.74	Treatment course	±20%	Lognormal (1.32, 0.48)	Colucci *et al.*, 2005[4]
Panitumumab	$1.50	Treatment course	±20%	Lognormal (0.18, 0.67)	Van Cutsem *et al.*, 2007[21]
Health state utilities					
Bevacizumab plus FOLFIRI	0.77	Treatment course	±20%	Beta (77, 100)	Whyte *et al.*, 2010[26]
Cetuximab plus FOLFIRI	0.77	Treatment course	±20%	Beta (77, 100)	Whyte *et al.*, 2010[26]
Panitumumab plus FOLFIRI	0.778	Treatment course	±20%	Beta (778, 1000)	Bennett *et al.*, 2011[27]
FOLFOX	0.756	Treatment course	±20%	Beta (756, 1000)	Bennett *et al.*, 2011[27]
Panitumumab	0.72	Treatment course	±20%	Beta (72, 100)	Odom *et al.*, 2011[28]
Best supportive care	0.68	Treatment course	±20%	Beta (68, 100)	Odom *et al.*, 2011[28]
Cancer-free	0.84	Treatment course	±20%	Beta (84, 100)	Van Cutsem *et al.*, 2009[29]
Dead	0				

TABLE II Continued

Variable	*Base-case value*	*Duration*	*Ranges tested in sensitivity*	*Probability distribution*	*Reference*
Transition probabilities					
Progression-free survival					
Bevacizumab plus FOLFIRI	Varying by month Γ=1.34, λ=16.45	Treatment course	±20%	Beta (varying by month)	NDFP
Cetuximab plus FOLFIRI	Varying by month Γ=1.34, λ=16.45	Treatment course	±20%	Beta (varying by month)	Van Cutsem *et al.*, 2011[19]
Panitumumab plus FOLFIRI	Varying by month	Treatment course	±20%	Beta (varying by month)	Douillard *et al.*, 2010[20]
FOLFOX	Varying by month	Treatment course	±20%	Beta (varying by month)	Colucci *et al.*, 2005[4]
FOLFOX plus bevacizumab	Varying by month	Treatment course	±20%	Beta (varying by month)	Colucci *et al.*, 2005[4]
Panitumumab monotherapy	Varying by month	Treatment course	±20%	Beta (varying by month)	Van Cutsem *et al.*, 2007[21]
Overall survival					
Best supportive care	Varying by month	Treatment course	±20%	Beta (varying by month)	Van Cutsem *et al.*, 2007[21]
Bevacizumab to cancer-free	0.001536953	Treatment course	±20%	Beta (15, 10000)	Ramsey *et al.*, 2000[25]
Cetuximab to cancer-free	0.003423096	Treatment course	±20%	Beta (34, 10000)	Van Cutsem *et al.*, 2009[10]
Panitumumab to cancer-free	0.008284798	Treatment course	±20%	Beta (83, 10000)	Douillard *et al.*, 2010[20]
Cancer recurrence	First 60 months	0.012392865	±20%	Beta (124, 10000)	Tomlinson *et al.*, 2007[30]
	Subsequent months	0.003733782	±20%	Beta (37, 10000)	Tomlinson *et al.*, 2007[30]
Discount rate			0.5	0%–0.5%	

OHIP = Ontario Health Insurance Plan; CIHI = Canadian Institute for Health Information.

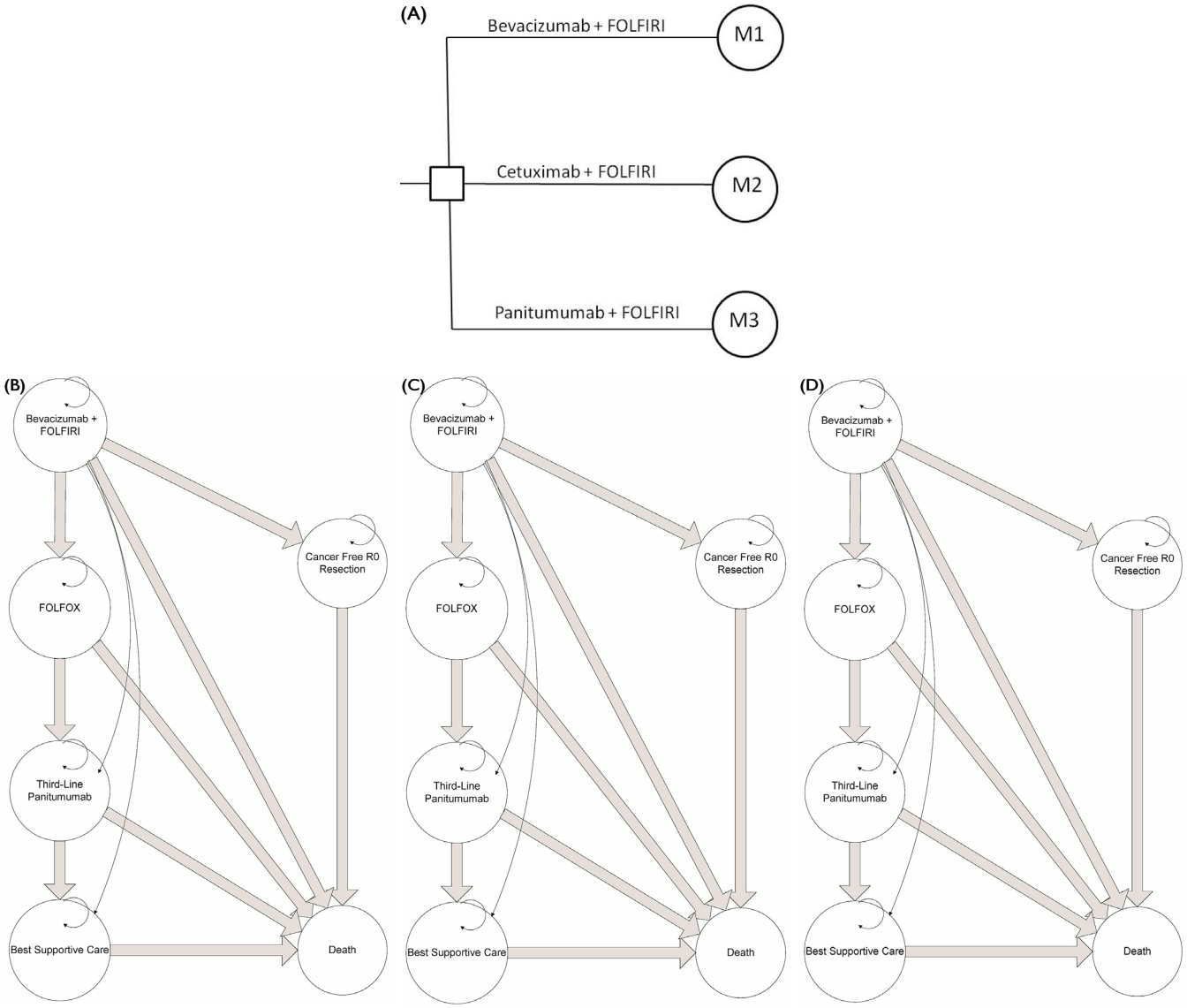

FIGURE 2 (A) The decision analytic model. (B) Markov model M1. (C) Markov model M2. (D) Markov model M3.

was then determined by multiplying those costs by the monthly probability for the occurrence of each adverse event determined from the overall adverse event rates taken from each clinical trial. In the study, all costs reflect 2012 Canadian dollars.

3. RESULTS

In the base case, bevacizumab plus FOLFIRI dominated the other two first-line treatment options. Compared with bevacizumab plus FOLFIRI, first-line treatment with panitumumab plus FOLFIRI resulted in an incremental loss of 0.033 QALYS per person at an incremental cost of $23,359; treatment with cetuximab plus FOLFIRI resulted in an incremental loss of 0.008 QALYS per person at an incremental cost of $3,159 (Table III).

3.1 Sensitivity Analyses

In one-way sensitivity analyses, we varied all parameters by ±20% of the base-case value. We found that the incremental cost-effectiveness ratio (ICER) was most sensitive to changes in the monthly transition probabilities, the costs of bevacizumab and cetuximab, and the health utility values of the first-line cetuximab and bevacizumab treatment options. First-line treatment consisting of cetuximab plus FOLFIRI was no longer dominated when patients receiving first-line bevacizumab plus FOLFIRI progressed more quickly (that is, when the monthly transition probabilities were increased) or when patients receiving first-line cetuximab plus FOLFIRI progressed more slowly (that is, monthly transition probabilities were

TABLE III Base-case results

Treatment	*Cost*	*QALY*	*ICER*
Bevacizumab plus FOLFIRI	$150,572	1.749	
Cetuximab plus FOLFIRI	$153,731	1.741	Dominated
Panitumumab plus FOLFIRI	$173,931	1.716	Dominated

QALY = quality-adjusted life-year; ICER = incremental cost-effectiveness ratio.

decreased). However, in both scenarios, the ICER values of first-line cetuximab plus FOLFIRI were more than $100,000 per QALY gained.

Treatment with cetuximab plus FOLFIRI turned out to be the most cost-effective treatment option when the cost of bevacizumab plus FOLFIRI was increased by 20%, or when the cost of cetuximab plus FOLFIRI was decreased by 10%. The ICER values for treatment with cetuximab plus FOLFIRI fell below $100,000 per QALY when either the utility of patients receiving first-line cetuximab plus FOLFIRI increased by 10% or the utility of patients receiving first-line bevacizumab plus FOLFIRI decreased by 10%. In all scenarios tested, treatment with panitumumab plus FOLFIRI was either dominated or had an ICER exceeding $159,615 per QALY.

We also performed a probabilistic sensitivity analysis, varying all parameters simultaneously using appropriate probability distributions (Table II). In a comparison with bevacizumab plus FOLFIRI, and using a willingness-to-pay threshold of $100,000 per QALY, first-line cetuximab plus FOLFIRI was the most cost-effective strategy in 0.4% of simulations, and treatment with panitumumab plus FOLFIRI was the most cost-effective in 0.2% of simulations [Figure 3(A,B)].

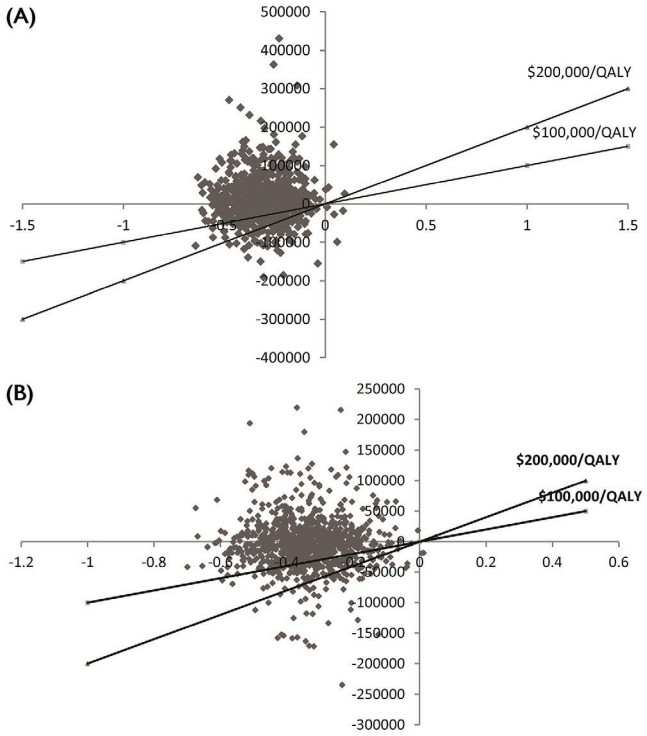

FIGURE 3 *Incremental cost-effectiveness scatter plots comparing (A) cetuximab plus FOLFIRI (leucovorin, 5-fluorouracil, irinotecan) with bevacizumab plus FOLFIRI, and (B) panitumumab plus FOLFIRI with bevacizumab plus FOLFIRI.*

4. DISCUSSION

We developed a decision analytic model to assess the cost-effectiveness of three first-line treatment strategies (bevacizumab plus FOLFIRI, cetuximab plus FOLFIRI, and panitumumab plus FOLFIRI) for patients with *KRAS* WT mCRC. In the base case, the treatment strategy of bevacizumab plus FOLFIRI dominated the two alternative treatment strategies. Although combinations of cetuximab or panitumumab with FOLFIRI or FOLFOX have been shown to improve patient outcomes compared with those achieved using FOLFIRI or FOLFOX alone, our analysis showed that such treatment strategies might not be cost-effective options when compared with current clinical practice—that is, bevacizumab plus FOLFIRI—for patients in Ontario.

Although it was dominated in the base case, cetuximab plus FOLFIRI is very similar to bevacizumab plus FOLFIRI as a treatment strategy in terms of both cost and effect, given certain choices for parameter values. The similarity of bevacizumab plus FOLFIRI and cetuximab plus FOLFIRI as first-line treatment strategies, together with the ICER values determined from sensitivity analyses of the health utility values, indicates that, in some settings, cetuximab plus FOLFIRI could potentially be a cost-effective treatment option for patients with *KRAS* WT mCRC. Specifically, if the utility of patients receiving bevacizumab plus FOLFIRI is decreased or the utility of patients receiving cetuximab plus FOLFIRI is increased, then cetuximab plus FOLFIRI emerges as a treatment option that is more cost-effective than bevacizumab plus FOLFIRI.

The use of panitumumab plus FOLFIRI was not cost-effective relative to the other two treatment strategies in any scenario that we evaluated. Although we did identify scenarios in which treatment with panitumumab plus FOLFIRI was not dominated, the ICER for its use never fell below $159,000 per QALY. Our analysis demonstrated that panitumumab plus FOLFIRI should not be considered for adoption as first-line treatment for patients with *KRAS* WT mCRC.

The results of the present study differ from those of two earlier studies[31,32]. In the study in Germany by Asseburg *et al.*[31], the cetuximab plus FOLFIRI combination, compared with bevacizumab plus FOLFOX, was found to have an ICER €15,020 per life-year gained. Taking the perspective of the National Health Service in the United Kingdom, Samyshkin *et al.*[32] found an ICER of £28,626 per QALY for cetuximab plus FOLFIRI

compared with bevacizumab plus FOLFOX. One possible reason for the differences in these estimates is that both studies included FOLFOX in the comparator, and FOLFOX is much more expensive than FOLFIRI because of the increased cost of oxaliplatin. Thus, some cost savings might have been associated with the use of FOLFIRI instead of FOLFOX, which might have resulted in lower ICER values. The FOLFOX–bevacizumab combination was not reimbursed by the province of Ontario during the time of our analysis, and thus we could not capture the implications of that regimen. Differences in the results might also be attributable to different modelling approaches, model assumptions, health utility values used, extrapolation methods, and data sources.

Our study has several limitations.

First, no randomized clinical trial data that provide a head-to-head comparison of the three treatment options in this patient population have yet been published. To compare the outcomes of patients receiving each treatment option over the course of their disease, we had to make indirect comparisons using data from published clinical trials, thus simulating patient outcomes over time as their disease progressed. A randomized clinical trial from Germany comparing FOLFIRI–bevacizumab with FOLFIRI–cetuximab in the first-line treatment of patients with *KRAS* WT MCRC has been presented in abstract form[33]. Despite the lack of a statistically significant difference in PFS between the two arms (10.3 months with FOLFIRI–bevacizumab vs. 10.0 months with FOLFIRI–cetuximab, $p = 0.547$), investigators describe an improvement in OS favouring cetuximab (28.7 months with FOLFIRI–cetuximab vs. 25.0 months with FOLFIRI–bevacizumab, $p = 0.017$).

Second, the same health utility value was used for patients whether they received first-line cetuximab–FOLFIRI or bevacizumab–FOLFIRI. It is possible that use of the same health utility values for both treatments might have had led to some bias in the final ICERS.

Third, given a restriction in the information provided in the Eastern Cooperative Oncology Group 3200 RCT, we were unable to use parametric methods to fit a Weibull distribution to the PFS curves for patients receiving second-line treatment (either FOLFOX or combination FOLFOX–bevacizumab); the estimates were therefore extrapolated using the average of the last 4 months of trial data. Also, using the patient-level data, we were able to determine only an estimate of PFS for patients receiving second-line FOLFOX. Given that the Eastern Cooperative Oncology Group 3200 clinical trial found that treatment with FOLFOX and bevacizumab was more effective than treatment with FOLFOX alone, it was not plausible to incorporate the administrative data for second-line treatment into our analysis, because it would have biased the final cost and effectiveness.

Finally, because of assumptions made concerning the start of the best supportive care treatment phase, the cost estimates for patients in the best supportive care state might not be fully accurate (all costs associated with that arm were not captured in the Ontario administrative data). However, given that the costs used for the best supportive care state were constant in all three treatment strategies, we do not expect that situation to have influenced the final ICER values.

5. CONCLUSIONS

We found that treatment with bevacizumab plus FOLFIRI dominates panitumumab plus FOLFIRI and cetuximab plus FOLFIRI in the context of the public payer model in Ontario. Given that genetic testing is necessary for the cetuximab plus FOLFIRI and panitumumab plus FOLFIRI options, but that such a test is not required for bevacizumab plus FOLFIRI treatment, excluding the cost of testing from the bevacizumab plus FOLFIRI option would make our conclusions even stronger. We thus recommend that the current clinical practice of using bevacizumab plus FOLFIRI should remain the preferred first-line treatment strategy for patients diagnosed with *KRAS* WT MCRC. Compared with the strategy of bevacizumab plus FOLFIRI, cetuximab plus FOLFIRI had very similar outcomes in terms of overall costs and expected QALYS under certain ranges of parameter choices. The cost-effectiveness of the cetuximab plus FOLFIRI option therefore requires further investigation in future research.

6. ACKNOWLEDGMENTS

We thank two anonymous reviewers for their helpful suggestions, which improved the manuscript. Our study was supported through provision of data by the Institute for Clinical Evaluative Sciences (ICES) and Cancer Care Ontario (CCO), and through funding support to ICES in the form of an annual grant from the MOHLTC and the Ontario Institute for Cancer Research (OICR). Funding for the present research by the Department of Epidemiology and Biostatistics, Schulich School of Medicine and Dentistry, Western University is gratefully acknowledged. This publication is a revised version of EME's Master of Science thesis submitted to Western University. The opinions, results and conclusions reported in this paper are those of the authors. No endorsement by ICES, CCO, OICR, the Government of Ontario, or other institution is intended or should be inferred.

7. CONFLICT OF INTEREST DISCLOSURES

The authors declare that there are no financial conflicts of interest.

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