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Toronto Health Economics and Technology Assessment Collaborative

Cost-effectiveness of KRAS Genetic Testing for Anti-EGFR Therapy in Metastatic Colorectal Cancer

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Executive Summary

Objectives

To evaluate the cost-effectiveness of KRAS genetic testing in the (third-line) treatment of metastatic colorectal cancer (mCRC) with two anti-EGFR agents used as monotherapies; cetuximab and panitumumab, and the combination therapy of cetuximab with irinotecan (chemotherapy). The cost-effectiveness of KRAS testing for each of the three treatment options was assessed individually, and the relative cost-effectiveness of all treatments when compared to each other was also examined.

Methods

The economic analysis consisted of: 1) a systematic review of existing literature examining economic evaluations of KRAS genetic testing for mCRC; 2) a cost-utility analysis and decision analytic (Markov) model evaluating genetic testing strategies for three treatment options of mCRC (cetuximab, panitumumab and cetuximab with irinotecan chemotherapy); and 3) a budget impact analysis assessing the cost effect from the perspective of the Ministry of Health and Long-Term Care (MOHLTC).

Results

For each of the three treatment options considered individually (cetuximab, panitumumab and cetuximab with irinotecan chemotherapy), KRAS genetic testing was considered cost-effective at a willingness-to-pay (WTP) threshold of $50-$60K CAD. When all treatment options and strategies were considered together and compared in a relative cost-effectiveness analysis, KRAS testing for cetuximab with irinotecan chemotherapy was the most cost-effective option; with the highest lifetime gain in quality-adjusted life years (QALYs) and lowest calculated ICER (~$43K per QALY). Probabilistic sensitivity analysis indicated that strategies with KRAS testing were 44% (panitumumab), 42% (cetuximab with irinotecan), and 14% (cetuximab) cost-effective for a WTP threshold of $50K per QALY. The average annual increase in budget (cost) of having 50% of mCRC patients seeking third-line treatment with cetuximab, panitumumab and cetuximab with irinotecan chemotherapy was calculated respectively as: $0.07M, -$1.76M (cost saving), and $1.63M.

Conclusions

KRAS genetic testing is cost-effective for currently available anti-EGFR therapies for the treatment of mCRC. Specifically, providing KRAS testing for treatment with cetuximab and panitumumab monotherapies, and cetuximab with irinotecan chemotherapy is cost-effective at a WTP threshold of $50-$60K. Current indications by Health Canada (and

Cancer Care Ontario) require KRAS testing for patients to gain access to the three anti-EGFR therapies evaluated in the current analysis. While not all KRAS testing strategies were found be equally cost-effective in the comparative analysis, KRAS testing should continue to provide benefit (in both cost and lifetime QALYs) for all three treatment therapies.

Overview

Study Question

The objective of the current economic analysis was to determine the cost effectiveness of k-RAS oncogene (KRAS) testing for the third-line treatment of (stage IV) metastatic colorectal cancer (mCRC) in Ontario. Third-line treatments used in this analysis consisted of the following drug regimens: cetuximab and panitumumab monoclonal anti-body (MoAb) anti-EGFR monotherapies, and cetuximab used in combination with irinotecan chemotherapy. Note that the comparative cost-effectiveness analysis focuses on the benefit of KRAS genetic testing – comparison was made between strategies showing the benefit of KRAS testing and not necessarily the benefit of drug treatments alone.

Economic Analysis

A decision-analytic cost-utility analysis (CUA) was conducted to evaluate the relative cost-effectiveness of testing for KRAS genetic mutations with subsequent treatment by four options: cetuximab monotherapy, panitumumab monotherapy, cetuximab in combination with irinotecan, and best supportive care (BSC). Best supportive care was defined identically as Jonker et al. 2007 as being: "... those measures designed to provide palliation of symptoms and improve quality of life as much as possible".(1) As the definition of BSC was synonymous with that defined by Jonker et al. 2007, cost parameters used for BSC as taken from Mittmann et al. 2009 (2) were consistent in terms of the definition of patient population.

The physician and hospital costs for the non-invasive imaging tests were taken from 2009 Ontario Health Insurance Plan (OHIP) and the Ontario Case Costing Initiative (OCCI) administrative databases.(3, 4) Costs of drug treatments were taken from publicly listed prices provided by the New Drug Funding Program (NDFP) as administered by Cancer Care Ontario (CCO); values provided were based on consultations with experts.

A budget impact analysis (BIA) was performed assessing the effect of replacing a certain proportion of patients (cases) with the drug regimen of interest; either cetuximab, panitumumab, or cetuximab in combination with irinotecan. The costs and volume of patients presented in this BIA were estimated from expert consultation and CCO data sources from 2009.

Background

Economic Literature Review

A literature search was performed on May 20th, 2010 using OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, OVID EMBASE, Wiley Cochrane, and EconLit. The range of dates used for the systematic search was: 1996 to Week 2 2010 for MEDLINE, and 1980 to Week 19 2010 for EMBASE. Included studies were those with full economic evaluations describing both costs and consequences of KRAS genetic testing for (stage IV) mCRC patients.

According to the systematic review performed, there were no health economic evaluations found comparing the relative cost-effectiveness of KRAS genetic testing for the population and therapies of interest. However, a CUA was done by Mittmann et al. in 2009 related to the results of the CO-17 trial conducted by Jonker et al. in 2007, which included patients from Ontario.(1, 2) Costs and effects (health-related quality-of-life utilities) specific to mCRC third-line patients receiving, separately, cetuximab monotherapy and BSC were taken from Mittmann et al. 2009 and used in the current economic evaluation and decision-analytic model.

Methodology

Target Population

The target population in this economic evaluation was defined as patients diagnosed with (stage IV) metastatic colorectal cancer (mCRC) from whom cetuximab or panitumumab monotherapies, or cetuximab and irinotecan combination therapy were indicated as third-line treatments. According to Health Canada this indication requires certain restrictions for patients for each treatment option as follows: a) for cetuximab monotherapy, patients must be intolerant to irinotecan, or have failed on both irinotecan- and oxaliplatin-based regimens and have received a fluoropyrimidine (chemotherapy) as previous treatments; b) for panitumumab monotherapy, patients must have failed on fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens; and c) for cetuximab and irinotecan combination therapy, patients must be refractory to other irinotecan-based chemotherapy regimens.(5, 6)

In addition to the restrictions listed above for the three treatment options considered in the current evaluation, patients must have tested negative for KRAS mutations (i.e. KRAS wild-type). It is important to note that for comparison purposes, certain strategies consisted of treating patients with KRAS mutations; while the benefit of KRAS genetic testing was the focus of the evaluation, treating mCRC patients with KRAS mutations using the three treatments above is not indicated in Ontario.

Perspective

The analytic perspective was that of the Ontario Ministry of Health and Long-Term Care (MOHLTC).

Comparators

The seven strategies listed in Table 1 were used to evaluate the benefit of KRAS genetic testing for third-line treatment(s) of mCRC:

0) Best supportive care (No KRAS test; No treatment)
1a) Cetuximab (Perform KRAS test)
1b) Cetuximab (No KRAS test)
2a) Panitumumab (Perform KRAS test)
2b) Panitumumab (No KRAS test)
3a) Cetuximab + Irinotecan (Perform KRAS test)
3b) Cetuximab + Irinotecan (No KRAS test)

Time Horizon

The time horizon used in the model was life-time in length (i.e. the model's patient cohort was followed until death).

Discounting

All costs and effects (quality-adjusted life years, or QALYs) were discounted at a common rate of 5% per annum (7).

Model Structure

A schematic of the Markov model is shown in Figure 1. Metastatic CRC Patients receiving third-line treatment with cetuximab, panitumumab or cetuximab and irinotecan combination therapy begin the Markov process in the health state labelled "Stable: No cancer progression". Subsequent state transitions were informed by the median overall survival time (OS) and progression-free survival time (PFS) for transitions to the "Dead" and "Un-stable: Cancer progression" health states, respectively. The model also incorporated adverse events (AEs) specific to each treatment as summarized in the Parameter Estimates section. Note that the cycle length in the Markov model was one month.

Outcomes

The outcome of interest was the lifetime-aggregated QALYs (per patient) associated with each strategy.

Resource Use and Costs

Costs were reported in 2009 Canadian dollars (CAD) and were taken from literature, 2009 OHIP and OCCI administrative databases. Table 2 summarizes the drug costs used in current the CUA, where an average value of 1.75 m^2 was used for Body Surface Area (BSA) and an average value of 64.1 kg was used for mass (body weight). The CCO prices listed under the "Reference" column were obtained through consultation with experts and publicly listed NDFP drug prices. Note that the cost per "cycle" refers to the one-month cycle used in the Markov model; actual drug cycles are listed under "Drug dose". The cost of the KRAS genetic test was taken from expert consultations and estimated as being $500 (range $150-$500).

Other treatment costs were estimated for patient management and the administration of MoAb and chemotherapy. BSC management costs were estimated from Mittmann 2009: approximately $61/month, based on an aggregated average of $1,093 over 18 months per patient.(2) The hospital cost of outpatient administration of MoAb treatment (cetuximab or panitumumab monotherapy) was estimated from FY2008 OCCI data as being $118. This was derived by subtracting the average drug cost per oncology visit ($92 (8)) from the

average cost reported for onocology outpatient functional centres ($210 (3)), where patients had: a most responsible diagnosis of chemotherapy (ICD-10-CA code of Z51.1 or Z51.2), and a principal procedure of monoclonal antibody targeted injection (CCI code of 8.NZ.70.HZ-CC).(9, 10) In a similar way, the hospital cost of outpatient administration of a MoAb with chemotherapy (cetuximab with irinotecan) was estimated as being $329 per patient (i.e. subtraction of $92 from $421, reported for ICD-10-CA codes of Z51.1 or Z51.2, together with CCI codes of 1.ZZ.35.HA-M0 to 1.ZZ.35.HA-M9).(9, 10) Oncology physician costs were estimated as being $132.50 per consultation and $64.05 per additional assessment, related to patient follow up and the treatment of potential adverse events.

The costs for certain AEs were estimated from the literature and hospital administrative databases. The cost of grade 3 or 4 AEs, as defined by criteria published by the National Cancer Institute Common Toxicity Criteria (11), was estimated for the following AEs: rash ($992.50; (2), pain ($27; Mittmann 2009), non-neutropenic infection ($2,340; Mittmann 2009), neutropenia ($4,645; medical oncology inpatient diagnosis code of D70.0; (10)), hypomagnesemia ($318; outpatient diagnosis code of E83.4; (10)), and diarrhea ($357; outpatient dehydration diagnosis code of E86.0 with infusion procedure codes 1.LZ.35.XX-C7, 1.LZ.35.XX-T9 and 1.LZ.35.XX-Z9, where "XX" can be HH, HA or HR; (9)).

Parameter Estimates

The effectiveness of treatments for third-line therapy for mCRC patients was summarized from the literature and shown in Table 3. Adverse events parameters are summarized in Table 4 and show the proportion of patients with the specified AE (grade 3 or 4 as defined by NCI-CTC). Note that the percentages were "normalized" and re-calculated such that the totals sum to 100% for the given list of AEs. Values related to BSC were taken from Jonker et al. 2007 and Karapetis 2008; values for cetuximab-related therapies were taken from Cunningham 2004, Jonker et al. 2007, Karapetis et al. 2008, and Loupakis et al. 2009; and values for panitumumab were taken from Van Cutsem et al. 2008 and Amado et al. 2008.(1, 12-16)

Quality-of-life utility weights used to calculate patient QALYs were based on literature estimates. A baseline utility value of 0.71 was assigned to all patients and was based on utility values reported for mCRC patients treated by only BSC as third-line therapy.(2) A utility increase of 0.07 associated cetuximab, panitumumab or cetuximab with irinotecan treatments was applied to patients for all strategies *except* BSC, and was calculated from Mittmann et al. using

4-24 week averaged utility values.(2) In a separate sensitivity analysis, the utility increase for panitumumab was estimated at 0.12 and taken from Siena et al.(17)

Sensitivity Analysis

A probabilistic sensitivity analysis (PSA) was conducted to assess the relative percentage cost-effectiveness of the KRAS testing strategies listed in the Comparators section for different willingness-to-pay (WTP) thresholds. The following is a list of strategies considered in the PSA: 0) Best supportive care (No KRAS test; No treatment); 1a) Cetuximab (Perform KRAS test); 2a) Panitumumab (Perform KRAS test); and 3a) Cetuximab + Irinotecan (Perform KRAS test). The range of parameter values used in the PSA is summarized in Table 5.

Results

Discussion

A summary of the results showing the benefit of KRAS genetic testing is presented in Table 6. All strategies considering KRAS testing for third-line treatment of mCRC disease were found to be cost-effective when compared to the corresponding strategies of no KRAS testing. Specifically, KRAS testing was found to be cost-effective for cetuximab monotherapy (at a WTP threshold of $54,802); KRAS testing was found to be cost-effective for panitumumab monotherapy (at a WTP threshold of $47,795); and KRAS testing was found to be cost-effective for cetuximab with irinotecan combination therapy (at a WTP threshold of $42,701).

When all treatment strategies were considered in the CUA simultaneously (Table 7), performing KRAS testing for cetuximab with irinotecan combination therapy was the preferred cost-effective option (at a WTP threshold of $42,710). For a WTP threshold of $50K, this strategy yielded the greatest effect (QALYs) and had the lowest ICER value. If a higher WTP threshold is considered, the strategy of not testing for KRAS genetic mutations is cost-effective at a WTP threshold of $163,396. This latter result was due to the combination treatment contributing QALYs (having beneficial effect) to both the KRAS wild-type and mutated patient groups. However, further research may be needed to determine the exact benefit of using cetuximab with irinotecan therapy on mCRC patients (both KRAS wild-type and mutated).

Results of the PSA (Figure 2) showed that for all strategies involving KRAS genetic testing, cetuximab with irinotecan combination therapy was the cost-effective option for increasing values of WTP. For lower WTP values, the probability of specific KRAS testing strategies being cost-effective varied. At a WTP of $50K, the probabilities of cetuximab monotherapy, panitumumab monotherapy and cetuximab with irinotecan combination therapy being cost-effective were approximately 14%, 44% and 42%, respectively. The strategy of not performing the KRAS test and treating patients with BSC alone was not cost-effective (zero probability) for WTP values greater than $45K.

Budget Impact Analysis

The BIA calculation of the current CUA was based on the number of drug claims reported by the NDFP and through consultations with experts. The number of mCRC patients using panitumumab as third-line therapy in Ontario in FY2009 was 145 according to the NDFP. The corresponding

number of cetuximab with irinotecan patients was about 38, however, the number of cetuximab monotherapy patients was unavailable as this treatment option is not funded by the NDFP and is available only out-of-country. It was assumed (expert consultation) that the distribution of treatments for third-line treatment of mCRC was approximately 30% for cetuximab, 20% for panitumumab and 30% for cetuximab with irinotecan combination therapy (and 30% for BSC for a total of 100%). Using these proportions, it was estimated that the number of patients using cetuximab monotherapy in 2009 was 218.

Using the average cost of treatments reported in Table 6 and Table 7, the impact of having 50% of patients on any given therapy was calculated for the BIA. The results are summarized in Table 8, where the "estimated FY2009 costs" were calculated from the current distribution of mCRC patients using third-line therapy (i.e. 30% cetuximab, 20% panitumumab, 30% cetuximab with irinotecan), and the "Re-calculated FY2009" costs were based on the re-calculated patient proportions or number of patients for the impact analysis. The effect of shifting patients, where 50% of mCRC patients would use the indicated third-line therapy in Table 8, was estimated as the simple difference between the estimated costs given the current distribution and the estimated (re-calculated) costs given the new distribution. As a result, estimates of the yearly cost savings (if any) of the different distributions of patients on a given third-line therapy were: a yearly increase of $0.07M for cetuximab, a yearly decrease of $1.76M for pantiumumab, and a yearly increase of $1.63M for cetuximab with irinotecan combination therapy.

Conclusion

KRAS genetic testing is cost-effective for currently available anti-EGFR therapies for the treatment of mCRC. Specifically, providing KRAS testing for treatment with cetuximab and panitumumab monotherapies, and cetuximab with irinotecan chemotherapy is cost-effective at a WTP threshold of $50-$60K. Current indications by Health Canada (and Cancer Care Ontario) require KRAS testing for patients to gain access to the three anti-EGFR therapies evaluated in the current analysis. While not all KRAS testing strategies were found be equally cost-effective in the comparative analysis, KRAS testing should continue to provide benefit (in both cost and lifetime QALYs) for all three treatment therapies.

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Exhibits

Tables

Table 1: Cost-effectiveness strategies evaluating the benefit of KRAS testing

Number	Label	Description
0	Best supportive care (No KRAS test; No treatment)	All patients were treated with BSC (i.e. no MoAb anti-EGFR therapy or chemotherapy)
1a	Cetuximab (Perform KRAS test)	In addition to BSC treatment, patients with KRAS wild-type received cetuximab monotherapy; patients with KRAS mutations received only BSC
1b	Cetuximab (No KRAS test)	All patients received both BSC and cetuximab monotherapy (i.e. this includes both KRAS wild-type and KRAS mutated patients)
2a	Panitumumab (Perform KRAS test)	In addition to BSC treatment, patients with KRAS wild-type received panitumumab monotherapy; patients with KRAS mutations received only BSC
2b	Panitumumab (No KRAS test)	All patients received both BSC and panitumumab monotherapy (i.e. this includes both KRAS wild-type and KRAS mutated patients)
3a	Cetuximab + Irinotecan (Perform KRAS test)	In addition to BSC treatment, patients with KRAS wild-type received cetuximab and irinotecan combination treatment; patients with KRAS mutations received only BSC
3b	Cetuximab + Irinotecan (No KRAS test)	All patients received both BSC and cetuximab and irinotecan combination treatment (i.e. this includes both KRAS wild-type and KRAS mutated patients)

Table 2: Drug costs (in CAD) used in the Markov model for third-line treatment of metastatic colorectal cancer (mCRC)

Treatment	Drug dose	Drug cost	Cost per cycle (month)	Reference
Cetuximab	400 mg/m^2 initial; 250 mg/m^2 weekly	$2,345; $1,466	$2,345; $5,862	CCO (NDFP price); $3.35/mg; BSA=1.75$m^2$
Panitumumab	6 mg/kg every 2 weeks	$2,308	$4,615	CCO (NDFP price); $6/mg; Average mass=64.1kg
Irinotecan	180 mg/m2 every 2 weeks	$158	$315	CCO (NDFP price); $0.50/mg; BSA=1.75$m^2$

Table 3: Treatment effectiveness parameters used in the Markov model

Treatment	KRAS status	Median PFS (months)	Median OS (months)	Reference
Best supportive care	WT + Mutated	1.8	4.6	(1)
Best supportive care	WT	1.9	4.8	(14)
Best supportive care	Mutated	1.8	4.6	(14)
Cetuximab	WT + Mutated	1.9	6.1	(1)
Cetuximab	WT	3.7	9.5	(14)
Cetuximab	Mutated	1.8	4.5	(14)
Panitumumab	WT + Mutated	2.4	6.3	(16)
Panitumumab	WT	3.1	8.1	(12)
Panitumumab	Mutated	1.8	4.9	(12)
Cetuximab + Irinotecan	WT + Mutated	4.1	8.6	(13)
Cetuximab + Irinotecan	WT	5.1	14.7	(15)
Cetuximab + Irinotecan	Mutated	3.8	9.7	(15)

Table 4: Selected grade 3 or 4 (NCI-CTC) adverse events and treatment-specific percent occurrences (normalized)

Treatment	Source	Rash	Abdominal Pain	Non-neutro. infection	Neutropenia	HypoMg	Diarrhea	Total %
Best supportive care	Original % from study	0.4%	15.7%	5.5%				21.6%
	Re-calculated % from selection of AE's	1.9%	72.7%	25.5%				100.0%
Cetuximab	Original % from study	11.8%	13.2%	12.8%		5.2%	2.0%	45.0%
	Re-calculated % from selection of AE's	26.2%	29.3%	28.4%		11.6%	4.4%	100.0%
Panitumumab	Original % from study	8.4%	7.4%				1.0%	
	Re-calculated % from selection of AE's	50.0%	44.1%				5.9%	
Cetuximab + Irinotecan	Original % from study	9.4%	3.3%		9.4%		21.0%	43.2%
	Re-calculated % from selection of AE's	21.9%	7.6%		21.9%		48.6%	100.0%

Table 5: Effectiveness, cost and utility parameter ranges used in the PSA analysis

Parameter	PFS Range (months)	OS Range (months)	Cost Range (per cycle)	Utility Range
Cetuximab - WT	1.40 - 5.40	6.60 - 10.80	$2,931 - $5,862	
Cetuximab - Mutated	1.30 - 4.40	4.50 - 9.50		
Panitumumab - WT	3.08 - 4.50	8.10 - 10.73	$2,308 - $4,615	0.07 - 0.12
Panitumumab - Mutated	1.83 - 1.85	4.90 - 5.55		
Cetuximab + Irinotecan - WT	3.90 - 8.00	10.80 - 20.80	$158 - $315	
Cetuximab + Irinotecan - Mutated	2.25 - 4.70	6.10 - 13.80		

Note: The cost ranges specified are general drug costs; the range specified for "Cetuximab + Irinotecan" actually refers to the cost of irinotecan only.

Table 6: Cost-effectiveness of KRAS genetic testing - treatment-specific results

Strategy	Cost	Incremental Cost	Effect (QALY)	Incremental Effect	ICER ($/QALY)
Cost-effectiveness of KRAS testing for cetuximab monotherapy					
0: BSC (No KRAS test; No treatment)	$1,414		0.7455		
1a: Cetuximab (Perform KRAS test)	$18,305	$16,891	1.0537	0.3082	54,802
1b: Cetuximab (No KRAS test)	$29,399	$11,094	1.0447	-0.0090	(Dominated)
Cost-effectiveness of KRAS testing for panitumumab monotherapy					
0: BSC (No KRAS test; No treatment)	$1,414		0.7455		
2a: Panitumumab (Perform KRAS test)	$12,236	$10,821	0.9719	0.2264	47,795
2b: Panitumumab (No KRAS test)	$20,424	$8,188	0.9985	0.0266	308,236
Cost-effectiveness of KRAS testing for cetuximab with irinotecan combination therapy					
0: BSC (No KRAS test; No treatment)	$1,414		0.7455		
3a: Cetuximab + Irinotecan (Perform KRAS test)	$23,373	$21,959	1.2596	0.5141	42,710
3b: Cetuximab + Irinotecan (No KRAS test)	$44,798	$21,425	1.3907	0.1311	163,396

Table 7: Relative cost-effectiveness of KRAS genetic testing for all treatment strategies

Strategy	Cost	Incremental Cost	Effect (QALY)	Incremental Effect	ICER ($/QALY)
0: BSC (No KRAS test; No treatment)	$1,414		0.7455		
2a: Panitumumab (Perform KRAS test)	$12,236	$10,821	0.9719	0.2264	(Ext.Dom.)
1a: Cetuximab (Perform KRAS test)	$18,305	$6,069	1.0537	0.0818	(Ext.Dom.)
2b: Panitumumab (No KRAS test)	$20,424	$2,119	0.9985	-0.0552	(Dominated)
3a: Cetuximab + Irinotecan (Perform KRAS test)	$23,373	$5,068	1.2596	0.2059	42,710
1b: Cetuximab (No KRAS test)	$29,399	$6,026	1.0447	-0.2149	(Dominated)
3b: Cetuximab + Irinotecan (No KRAS test)	$44,798	$21,425	1.3907	0.1311	163,396

Note: "Ext. Dom." represents strategies which are ruled out due to extended dominance.

Table 8: Cost differences between the current distribution of treatments and future 50%-distributions

Strategy	Patients (%)	Re-calculated patients (N)	Estimated FY2009 costs	Re-calculated FY2009 costs	Impact (cost difference)
Assuming 50% of patients are using cetuximab monotherapy					
1a: Cetuximab (Perform KRAS test)	**50%**	363	$3.98M	$6.64M	$2.65M
2a: Panitumumab (Perform KRAS test)	10%	73	$1.77M	$0.89M	-$0.89M
3a: Cetuximab + Irinotecan (Perform KRAS test)	10%	73	$3.39M	$1.69M	-$1.69M
Total	*70%*	*508*	*$9.14M*	*$9.22M*	*$0.07M*
Assuming 50% of patients are using panitumumab monotherapy					
1a: Cetuximab (Perform KRAS test)	12%	87	$3.98M	$1.59M	-$2.39M
2a: Panitumumab (Perform KRAS test)	**50%**	363	$1.77M	$4.44M	-$2.66M
3a: Cetuximab + Irinotecan (Perform KRAS test)	8%	58	$3.39M	$1.38M	-$2.03M
Total	*70%*	*508*	*$9.14M*	*$7.38M*	*-$1.76M*
Assuming 50% of patients are using cetuximab with irinotecan combination therapy					
1a: Cetuximab (Perform KRAS test)	12%	87	$3.98M	$1.59M	-$2.39M
2a: Panitumumab (Perform KRAS test)	8%	58	$1.77M	$0.71M	-$1.06M
3a: Cetuximab + Irinotecan (Perform KRAS test)	**50%**	363	$3.39M	$8.47M	$5.08M
Total	*70%*	*508*	*$9.14M*	*$10.77M*	*$1.63M*

Figures

Figure 1: KRAS CEA Markov model showing the three health states and possible state transitions

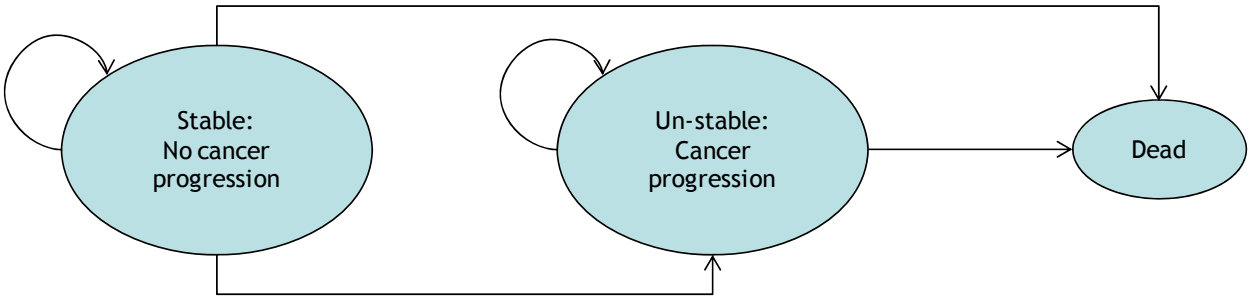
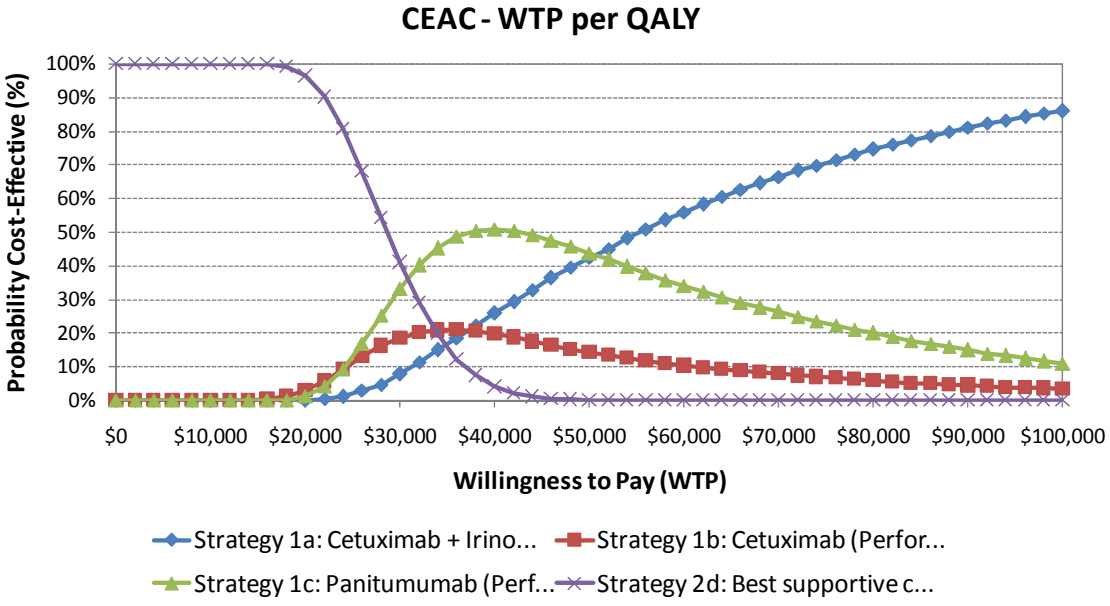


Figure 2: Cost-effectiveness acceptability curve showing the percent cost-effectiveness of strategies containing KRAS genetic testing



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