Targeted Therapies for Metastatic Colorectal Cancer: A Systematic Review of Cost Effectiveness

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Background

- Targeted therapies interfere with molecular mechanisms in order to reduce tumor growth and slow disease progression.
- Currently three targeted agents (bevacizumab, cetuximab, and panitumumab) have Food and Drug Administration approval for the treatment of metastatic colorectal cancer (mCRC).
- Choosing among agents to treat mCRC requires balancing efficacy, safety, quality of life, and, in cost-constrained systems, cost.

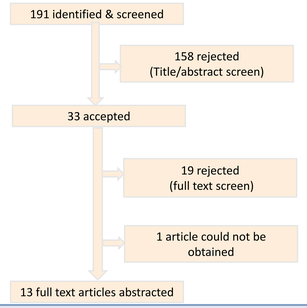
Objectives

This study aims to determine the most cost effective targeted therapy for mCRC.

Methods

- Systematic review of published studies of cost effectiveness of treatments for mCRC.
- Inclusion criteria: English language studies of adults with mCRC published between 2004-2011 (for manuscripts) or 2009-2011 (for abstracts). Studies must have included systemic targeted therapy and reported cost effectiveness outcomes from a payer or societal perspective.
- Databases searched: Medline, CancerLit, EMBASE, Cochrane, CINAHL, BIOSIS, Web of Science, Tufts CEA registry, ASCO and ASCO GI Conference Proceedings
- Keywords: colorectal neoplasms, antineoplastic agents, drug therapy, bevacizumab, cetuximab, panitumumab, cost analysis, economics, cost effectiveness, cost utility, cost consequence, cost minimization
- Incremental CE ratios (ICERs) were converted to US$ using 2010 purchasing power parity.
- All accepted articles were evaluated for quality using a validated instrument, the Quality of Health Economic Analyses (QHES).

Results



Results

Table 1: First line CEA models

Publication/Yr	Population	Comparators	ICER (US$)		QHES Score
			Per QALY	Per LY	
Cetuximab vs:					
Chemotherapy			**$38,574 ***		
Griebsch 2010	KRAS WT; LOM	Cet+FOLFIRI/FOLFOX vs. FOLFIRI/FOLFOX	$31,238	-	-
NICE #176 2009	KRAS WT; LOM; ECOG 0-1	Cet+FOLFIRI vs. FOLFIRI; Cet+FOLFOX vs. FOLFOX	$38,648	-	80
Samyshkin 2011	KRAS WT; LOM	Cet+FOLFIRI vs. FOLFIRI	$45,837	-	-
Bevacizumab			**$26,347 ***		
Asseburg 2011	KRAS WT; LOM	Cet+FOLFIRI vs. Bev+FOLFOX	-	$17,671	100
Samyshkin 2011	KRAS WT; LOM	Cet+FOLFIRI vs. Bev+FOLFOX	$26,347	-	-
Panitumumab			**$22,909***		
Samyshkin 2011	KRAS WT; LOM	Cet+FOLFIRI vs.Pan+FOLFOX	$22,909	-	-
Bevacizumab vs:					
Chemotherapy			**$101,891 ***		
Wong 2009	All mCRC	Bev+FOLFIRI vs. FOLFIRI	-	$174,118	100
NICE #118a 2007	All mCRC	Bev+IFL vs. IFL	$109,378	$81,530	93
NICE #118b 2007	All mCRC	Bev+5-FU/FA vs. 5-FU/FA	$154,273	$147,226	93
NICE #118c 2007	All mCRC	Bev+IFL vs. IFL	$154,123	$124,960	100
NICE #118d 2007	All mCRC	Bev+5-FU/FA vs. 5-FU/FA	$99,122	$84,339	100
NICE #212a 2010	Prev untreated mCRC	Bev+FOLFOX vs. FOLFOX	$168,543	-	76
NICE #212b 2010	Prev untreated mCRC	Bev+XELOX vs. XELOX	$163861	-	76
Villa 2010	Prev untreated mCRC	Bev+Iri or Oxavs. Iri or Oxa	$52,787	$13,197	-
Shiroiwa 2007	All mCRC	Bev + IFL, FOLFOX6, FU/LV, bFOL, or CAPOX vs. each alone	-	$117,077	91

LOM=Liver-only metastasis; Cet=Cetuximab, Bev=Bevacizumab; Iri=Irinotecan; Oxa=Oxaliplatin; BSC=Best supportive care

** Numbers represent the average value for that particular comparison*

Table 2: Second line CEA models

Publication/Yr	Population	Comparators	ICER (US$)		QHES Score
			Per QALY	Per LY	
Cetuximab vs:					
Best supportive care			**$207,733***	**$179,087***	
Starling 2007	Failed 2nd-line	Cet+Iri vs. ASC/BSC	$95,339	$71,122	84
Mittmann 2009	Chemo-refractory; KRAS WT	Cet+BSC vs. BSC	$160,723	$103,322	100
NICE #118c 2007	Iri-refractory	Cet+Iri vs. ASC/BSC	$367,137	-	100
NICE #118e 2007	Iri-refractory; Oxa-intolerant	Cet+Iri vs. ASC/BSC	$77,687	-	100
Norum 2006	All mCRC	Cet+Iri vs. BSC	-	$362,818	73
Chemotherapy				$104,254	
Annemans 2007	All mCRC	Cet+Iri vs. Standard of care	-	$34,390	84
Wong Cancer 2009	All mCRC	Cet+FOLFOX vs. FOLFOX	-	$174,118	100
Bevacizumab vs:					
Chemotherapy				**$121,025***	
Shiroiwa 2007	All mCRC	Bev+FOLFOX4 vs.FOLFOX4	-	$121,025	91

Cet=Cetuximab, Bev=Bevacizumab; Iri=Irinotecan; Oxa=Oxaliplatin; BSC=Best supportive care

** Numbers represent the average value for that particular comparison*

- Models described included studies done in 10 countries (# publications if >1): Belgium; Canada (3); Germany; Japan; Netherlands; Norway; South Korea (2); Sweden; US (3); UK (8)
- Years: 2006-2011
- Quality scores (as measured by the QHES) of the models ranged from 73-100. QHES could not be completed for abstracts.
- All four models evaluating cetuximab in first line therapy, and one of the six in subsequent lines of therapy, were done among biomarker-selected KRAS wild type patients.

Limitations

- All included CEAs had at least some limitations including pooling of data from studies with different designs, imbalance in the number of patients across trial arms, and use of less than optimal comparators.
- Some models used flawed inputs including median instead of mean survival and use of highly uncertain data. Some studies considered non standard treatments or considered a very limited population, thereby limiting the generalizability of the results.
- Most studies considered results among the same lines and comparators but with varying patient populations
- No models evaluated all three targeted agents simultaneously

Conclusions

- Lower ICERs appear to be associated with the use of a predictive biomarker and/or identification of a subpopulation (such as those with potentially resectable liver metastasis) that has a greater treatment benefit.
- In this context, cetuximab appears to be the most cost-effective targeted agent in 1st line mCRC treatment.
- Cetuximab's cost effectiveness in 1st line therapy was driven by its ability to convert initially unresectable liver metastasis to resectable.
- In 2nd or later lines, direct CEA comparisons among the three approved targeted agents in comparable biomarker-selected patients are needed to determine the most cost effective agent.

Future models should evaluate:

- Various patient populations and sub-populations (e.g., KRAS WT and mutant; chemo-refractory; older patients; patients with metastases confined to the liver)
- All targeted agents: brivanib; bevacizumab; cetuximab; panitumumab
- Data based on rigorous methodology and valid sources
- Cost, quality-of-life, and utilization assumptions and data that accurately reflect the full impact of therapy
- A wide range of sensitivity analyses that address a variety of assumptions

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