Direct Cost Survival Analysis of Treatment of Metastatic Colorectal Cancer

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Abstract

Background

Paclitaxel and metronomic colorectal cancer (mCRC) treated with 5-fluorouracil plus oxaliplatin (FOLFOX) have a median life expectancy (LE) of approximately 2 years. The addition of oxaliplatin, cetuximab and bevacizumab has increased LE significantly. Although they have been widely adopted, little is known about the financial impact of these new drugs.

Methods

Using published reports and aggregate data from NCTTs, we developed a Stylized Markov Model which assumes forward progression through therapy. Patients enter at time of choice of front line therapy and transition from state to state at one week intervals. In this analysis, drug costs are based on Average Sales Price. No other direct or indirect costs have been incorporated (upcoming).

Possible Treatment Sequences for Metastatic Colorectal Cancer

1) FOLFIRI, 2) Irinotecan, 3) Irinotecan and Cetuximab

Conclusions

Our model suggests that the survival advantage afforded by new therapies is contingent on treatment-related costs that may exceed current health care expenditures. The relative cost-effectiveness of new combination regimens compared to single agent drugs has not yet been established.

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References


Treatment Related Costs have increased with Introduction of New Agents

Model Inputs

Model Assumptions

70 yrs male 70 kg, 1.7 m2
Maximum of three lines of therapy
Parents alive at the end of each interval get equal “credit”
One dose reduction allowed prior to changing therapy
Dose reductions/cuts are translated into a 20% dose reduction
Costs only include drug costs (ASP)

Calculation of Probabilities

Sensitivity Analyses (Two Way)

Two Dimensional Sensitivity Analyses

Two- dimensional analyses were performed on model parameters to determine the impact of new drug introduction on C/E ratios. 

Potential Treatment Sequences for Metastatic Colorectal Cancer

1) FOLFIRI, 2) Irinotecan, 3) Irinotecan and Cetuximab

Limitations

Model uses aggregate data from multiple studies rather than patient level data
Results

Cost-Effectiveness Frontier: Baseline Analysis

Time on Treatment by Regimen

Stylized Markov Model

Patients enter at time of choice of front line therapy and transition from state to state at one week intervals. The Markov model assumes forward progression through up to three lines of therapy compared to 5FU/LV alone. Treatment strategies are based on progression and dose-limiting toxicity. Drug costs are based on Average Sales Price. No other direct or indirect costs are included. Model assumptions are defined at 60% of standard doses. Sensitivity analyses (SA) were performed on key variables.

Issue of Cost Effectiveness is Debated

Historical: $50,000/QALY (cost of one year of dialysis in the 1970s)
NEJM 2005 Analysis of ICDs--$100,000/QALY

CE Ratio/week compared to 5FU/LV
FOLFOX 8.7
FOLFIRI 4.7
Irino/Bev 5.8
Irino/Cex 7.0

The greatest impact of CE ratios

Stable Disease on Front Line Rx

Stable Disease on Second Line Rx

Markov Model

Survival=e-rate*time
Rate=(ln(0.5)/-Time in Months)/4.33

Limitations

Model uses aggregate data from multiple studies rather than patient level data

Neurotoxicity and Progression varied over beta distribution

Costs varied over continuous distribution between 20% and 100% of ASP

Incorporation of new agents into current model will be forthcoming.

Conclusions

Based on a 70 year old, 70 kg male with a BSA 1.7m2.