Pharmacoeconomic analysis of capecitabine versus 5-fluorouracil/leucovorin as adjuvant therapy for stage III colon cancer in Taiwan

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
The objective was to assess the cost-effectiveness of oral capecitabine, compared with intravenous bolus 5-fluorouracil and leucovorin, in the additional treatment of stage III colon cancer in Taiwan. The authors concluded that capecitabine not only improved health outcomes but also saved costs, from the perspective of the Bureau of National Health Insurance. There were a few limitations and some of the methods and results were not fully reported. The authors’ conclusions should be considered with caution.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of oral capecitabine, compared with intravenous bolus 5-fluorouracil and leucovorin, in the additional treatment of stage III colon cancer in Taiwan.

Interventions
Oral capecitabine was compared with intravenous bolus 5-fluorouracil and leucovorin, as adjuvant therapy.

Location/setting
Taiwan/secondary and tertiary care.

Methods
Analytical approach:
The analysis was based on a health-state transition model, with three main discrete disease states: stable disease, progressive disease, and death. The five time horizons included the 24-week treatment period plus three, four, five, or 10 years, or lifetime. The model included a hypothetical cohort of 100 patients. The authors stated that the perspective was that of the Bureau of National Health Insurance (BNHI) in Taiwan.

Effectiveness data:
The effectiveness data came from a phase III study (the Xeloda in adjuvant colon cancer therapy, X-ACT, study) that compared capecitabine with 5-fluorouracil and leucovorin (Twelves, et al. 2005, see ‘Other Publications of Related Interest’ below for bibliographic details). This provided estimates of the time spent in each health state for the hypothetical cohort using the partitioned survival of the clinical trial data and an intention-to-treat analysis. A log-normal distribution was used to extrapolate the clinical endpoints beyond the follow-up period, which was a median of 3.8 years.

Monetary benefit and utility valuations:
The utility values were from published literature. It was assumed that there was no difference in utility over the 24-week chemotherapy period between the two treatments. The authors divided the period after treatment into two sections (pre-relapse and post-relapse) to reflect the difference in utility.

Measure of benefit:
Benefit was measured in life-months and quality-adjusted life-months (QALMs). Future benefits were discounted at an annual rate of 3%.
Cost data:
The direct medical costs included those of chemotherapy drug acquisition and administration, managing treatment-related adverse events, and post-treatment care. The resource use assumptions came from an expert panel of 12 Taiwanese colorectal surgeons and medical oncologists and the a UK cost-effectiveness analysis of the X-ACT study. The chemotherapy drug unit costs were from the 2006 BNHI reference list and the unit costs of consultations, drug infusion, hospital stay, and accident and emergency visits were from the 2006 BNHI fee schedule for medical services. Post-treatment costs were from a study of terminal care, or the expert panel. All costs were expressed in Taiwan dollars (TWD) at 2007 values. Future costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
One-way sensitivity analyses were performed by varying the values for key model inputs by ±20%, including the costs for chemotherapy drugs, medication costs for adverse events, drug administration costs, utilities, and discount rates.

Results
The projected survival gains with capecitabine treatment were 0.48 QALMs at three years, 0.75 QALMs at four years, 1.04 QALMs at five years, 2.51 QALMs at 10 years, and 7.03 QALMs over a lifetime.

The cost savings with capecitabine were TWD 125,934 at three years, TWD 126,097 at four years, TWD 125,686 at five years, TWD 121,001 at 10 years, and TWD 103,940 over a lifetime.

The sensitivity analyses supported these findings and suggested that they were robust.

Authors’ conclusions
The authors concluded that capecitabine not only improved health outcomes but also saved costs, compared with 5-fluorouracil and leucovorin, from the perspective of the BNHI in Taiwan.

CRD commentary
Interventions:
The interventions were briefly reported. No explicit justification for the comparator was provided, but it seems that 5-fluorouracil and leucovorin was the usual treatment in the authors’ setting.

Effectiveness/benefits:
The authors did not give details of the design of the phase III clinical study that supplied the clinical estimates. No systematic search of the literature was reported, so it is unclear whether other relevant clinical data existed. The study that supplied the utility values was referenced, but no further details, such as the method of elicitation or population, were given, which reduces the transparency of the analysis.

Costs:
The costs were appropriately presented. It appears that all the categories of costs relevant to the selected perspective were included. The price year was not clearly stated. Some values seem to have been from 2006, while others were from a 2002 publication and it was unclear whether adjustments were made. For some costs, an expert panel survey was used and this might bias these estimations.

Analysis and results:
A display of the study design was included, but there was no diagram of the model itself, and the model structure was not described in detail. A synthesis of the costs and benefits was not required because capecitabine dominated the alternative, as it saved costs and was more effective. Uncertainty was partially investigated in a deterministic analysis, but the results were not fully presented; only the incremental results were reported. A probabilistic sensitivity analysis could have captured the overall parameter uncertainty more thoroughly. The authors briefly discussed some study limitations including the lack of Taiwanese utility data and that resource use was based on a local expert panel survey. The authors compared their results with those of other published studies and they were similar.

Concluding remarks:
There were a few limitations to the study and some of the methods and results were not fully reported. The authors’ conclusions should be considered with caution.
Funding
Funded by Roche Products Ltd, Taiwan, manufacturer of capecitabine.

Bibliographic details
Hsu TC, Chen HH, Yang MC, Wang HM, Chuang JH, Jao SW, Chiang HC, Wen CY, Tseng JH, Chen LT.
Pharmacoeconomic analysis of capecitabine versus 5-fluorouracil/leucovorin as adjuvant therapy for stage III colon cancer in Taiwan. Value in Health 2011; 14(5): 647-651

PubMedID
21839401

DOI
10.1016/j.jval.2011.01.010

Original Paper URL
http://www.valueinhealthjournal.com/article/S1098-3015(11)01325-8/abstract

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Administration, Oral; Antimetabolites, Antineoplastic /administration & dosage /economics; Antineoplastic Combined Chemotherapy Protocols /economics /therapeutic use; Capecitabine; Chemotherapy, Adjuvant; Colonic Neoplasms /drug therapy /economics /mortality /pathology; Cost Savings; Cost-Benefit Analysis; Deoxycytidine /administration & dosage /analogs & derivatives /economics; Drug Costs; Fluorouracil /administration & dosage /analogs & derivatives /economics; Health Resources /economics /utilization; Health Services Research; Humans; Kaplan-Meier Estimate; Leucovorin /administration & dosage /economics; Models, Economic; National Health Programs /economics; Neoplasm Staging; Outcome and Process Assessment (Health Care) /economics; Quality-Adjusted Life Years; Survival Rate; Taiwan; Time Factors; Treatment Outcome

AccessionNumber
22011001589

Date bibliographic record published
22/02/2012

Date abstract record published
09/10/2012