Cost-effectiveness of UGT1A1 genotyping in second-line, high-dose, once every 3 weeks irinotecan monotherapy treatment of colorectal cancer

Obradovic M, Mrhar A, Kos M

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 cost-effectiveness of uridine diphospho-glucuronosyltransferase 1A1 genotyping was evaluated, in second-line high-dose, irinotecan monotherapy, once every three weeks, for metastatic colorectal cancer patients. Genotyping with reduced initial irinotecan dose for 7/7 genotype patients was cost saving for African and Caucasian patients, but not cost-effective for Asian patients. Genotyping and additional prophylaxis with granulocyte-colony stimulating factors for 7/7 genotype patients was not cost-effective. The methodology was valid, but was not extensively reported. The authors’ conclusions should be treated with caution.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The aim was to compare the cost-effectiveness of treatment approaches based on genotyping of the hepatic uridine diphospho-glucuronosyltransferase 1A1 (UGT1A1) enzyme, for patients who had metastatic colorectal cancer and had recently started second-line, high-dose, irinotecan monotherapy once every three weeks.

Interventions
Three management strategies were compared.

In the first strategy no UGT1A1 genotyping occurred and the same treatment was given to all patients. If severe neutropenia occurred, the chemotherapy dose was reduced.
In the second strategy, UGT1A1 genotyping was used and a reduced initial irinotecan dose was given to UGT1A1 7/7 genotype patients, who were at increased risk of severe neutropenia.
In the third strategy, UGT1A1 genotyping was used and the standard initial irinotecan dose was administered to the UGT1A1 7/7 genotype patients, in combination with granulocyte-colony stimulating factor (G-CSF) to reduce the risk of neutropenia.

Location/setting
USA/secondary care.

Methods
Analytical approach:
A decision analytic model was used and populated with data from the literature. The time horizon was from the initiation of second-line chemotherapy until the patient’s death, which was less than a year on average. The authors reported that the US health care payer perspective was adopted.

Effectiveness data:
The effectiveness data were derived from published studies. Some assumptions were required and were reported. The primary clinical outcomes were severe neutropenia based on the patients’ genotype and treatment option, and the mean overall survival.

Monetary benefit and utility valuations:
Measure of benefit:
The authors used life-years gained (LYG) and cases of severe neutropenia prevented as the measures of benefit.

Cost data:
The economic analysis included the costs of UGT1A1 genotyping, second-line cancer treatment with irinotecan, treatment of grade 3/4 neutropenia, and prophylactic treatment with G-CSF. These costs were derived from the published literature. They were adjusted and reported for the price year 2006 in US dollars ($). All assumptions were reported.

Analysis of uncertainty:
The parameter uncertainty was investigated using probabilistic sensitivity analysis.

Results
An incremental analysis was performed and the results were presented separately for patients of African, Asian, and Caucasian origin, for a cohort of 100 patients.

Compared with no UGT1A1 genotyping, genotyping with a reduction in the initial irinotecan dose for 7/7 genotype patients was less costly and more effective in terms of severe neutropenia prevented and LYG for African and Caucasian patients. For Asian patients, the incremental cost-effectiveness ratio (ICER) was $6,818,203 per LYG.

The probability that genotyping was cost-effective in LYG was almost 100% for African patients and 75% or more for Caucasian patients, at various willingness-to-pay thresholds, while it was almost 0% for Asian patients.

Compared with no UGT1A1 genotyping, genotyping with prophylactic G-CSF for 7/7 genotype patients had an ICER above $3 million in all ethnic groups and a low probability (less than 10%) of being cost-effective at various willingness-to-pay values.

Authors’ conclusions
The authors concluded that genotyping followed by an initial reduced dose of irinotecan for UGT1A1 7/7 genotype patients was cost saving for African and Caucasian patients, but not cost-effective for Asian patients. Genotyping followed by the standard initial irinotecan dose and prophylactic treatment with G-CSFs for UGT1A1 7/7 genotype patients was not cost-effective for any ethnic population.

CRD commentary
Interventions:
The authors justified their selection of the comparators and UGT1A1 genotyping was recommended by clinical guidelines in the US setting to guide treatment.

Effectiveness/benefits:
The effectiveness data were from published studies, but no systematic review of the literature was reported. No information on the design or other characteristics of the primary studies was provided. The absence of these details means that an objective assessment of the validity of these clinical inputs is not possible.

Costs:
The categories of costs reflected the perspective adopted. The unit costs and resource quantities were not presented separately, which will prevent the analysis being easily reworked for other settings. The authors made several assumptions, which were reported. The price year and adjustments for inflation were reported.

Analysis and results:
The synthesis of the costs and benefits was appropriately performed by incremental analysis. The issue of uncertainty was adequately addressed using probabilistic sensitivity analysis. The results of the base case and the sensitivity analysis were clearly reported. The authors discussed the results of other clinical studies, in relation to the effectiveness
estimates used in their analysis, but they did not discuss any limitations to their study.

Concluding remarks:
Overall, the methodology was valid, but was not extensively reported and the authors' conclusions should be treated with caution.

Funding
No financial support received from any company involved in colorectal cancer treatment.

Bibliographic details

PubMedID
18466101

DOI
10.2217/14622416.9.5.539

Original Paper URL
http://www.futuremedicine.com/doi/abs/10.2217/14622416.9.5.539

Indexing Status
Subject indexing assigned by NLM

MeSH
Camptothecin /administration & dosage /analogs & derivatives /economics; Cohort Studies; Colorectal Neoplasms /drug therapy /economics /genetics; Cost-Benefit Analysis; Drug Administration Schedule; Genotype; Glucuronosyltransferase /economics /genetics; Humans

AccessionNumber
22008101055

Date bibliographic record published
13/05/2009

Date abstract record published
03/03/2010