Cost-effectiveness of UGT1A1*28 genotyping in preventing severe neutropenia following FOLFIRI therapy in colorectal cancer


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 aim was to assess the cost-effectiveness of screening for polymorphism in the UGT1A1*28 genotype before starting chemotherapy for patients with metastatic colorectal cancer. The authors concluded that screening was likely to be cost-effective, for the hospital. The methods seem to have been appropriate, but there were a few limitations. The authors’ conclusions appear to be appropriate for their setting.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The aim was to assess the cost-effectiveness of screening for polymorphism of the UGT1A1*28 variant of the UGT1A1 gene, prior to the initiation of chemotherapy in patients with metastatic colorectal cancer.

Interventions
UGT1A1*28 genotyping was compared with no genotyping for patients with metastatic colorectal cancer.

With no genotyping, patients with no haematological side-effect during the first course of combined 5-fluorouracil, leucovorin, and irinotecan (FOLFIRI) received the same dose 15 days later for the second course of treatment. Patients with grade three or four neutropenia during the first course, received a FOLFIRI dose reduced by 25% for the second course. Those with febrile neutropenia during the first course, switched to combined 5-fluorouracil, leucovorin, and oxaliplatin (FOLFOX).

With genotyping, patients found to be homozygous for the UGT1A1*28 variant (genotype 7/7) were given colony-stimulating factor to reduce the risk of chemotherapy-induced neutropenia during the first course of FOLFIRI, and then received the same FOLFIRI dose 15 days later. Patients with the variants UGT1A1*1/*1 (genotype 6/6) and *1/*28 (genotype 6/7) were given no prophylaxis and the same treatment as those who were not genotyped.

Location/setting
France/secondary care.

Methods
Analytical approach:
A decision-tree model was used and populated with data from the literature. The time horizon was from the initiation of genotyping until the end of the second course of chemotherapy. The authors reported that a hospital perspective was adopted.

Effectiveness data:
The effectiveness data were from published studies. The estimated probabilities for each outcome were identified by literature review in the MEDLINE database. The primary clinical outcome was the probability that patients would have a haematological side-effect, given their genotype and the treatment received.

Monetary benefit and utility valuations:
Measure of benefit:
The benefit measure was the number of cases of febrile neutropenia avoided in patients with genotype 7/7 who received prophylaxis, minus the difference between the number of febrile neutropenia cases occurring with genotyping versus without genotyping; cases avoided in genotyping arm – (cases occurring in the genotyping arm – cases occurring in the no genotyping arm).

Cost data:
The economic analysis included the costs of genotyping, chemotherapy, and hospitalisation for febrile neutropenia. These costs were from the accounts department of a French university hospital and they were in 2006 Euros (EUR).

Analysis of uncertainty:
The parameter uncertainty was investigated using probabilistic sensitivity analysis and one-way sensitivity analysis.

Results
The genotyping strategy avoided 91 febrile neutropenia cases, compared with no genotyping. The incremental costs per 1,000 patients for genotyping over no genotyping were EUR 85,800 for patients without co-morbidities and EUR 99,200 for patients with co-morbidities.

The incremental cost-effectiveness ratio was EUR 943 per febrile neutropenia case avoided for patients without co-morbidities and EUR 1,090 per febrile neutropenia case avoided for patients with co-morbidities.

The one-way sensitivity analysis found that varying the risk of haematological toxicity had a significant effect on the incremental cost-effectiveness ratio.

Authors' conclusions
The authors concluded that screening for UGT1A1 genotype polymorphism before chemotherapy for metastatic colorectal cancer was likely to be cost-effective, for the hospital.

CRD commentary
Interventions:
The selection of the comparators appears to have been appropriate and they were described.

Effectiveness/benefits:
It was reported that a literature review was conducted, but only one database was searched. It was unclear if the review was systematic, making it uncertain if all the best available evidence was used. No justification was given for the formula used to derive the measure of benefit. It was unclear how generalisable this measure of benefit would be to other studies.

Costs:
The categories of costs appear to have reflected the perspective adopted. The unit costs and resource quantities were presented separately, making the analysis easy to rework for other settings. The source for the cost data was reported clearly, but the use of costs from one hospital might reduce the generalisability of the study. The cost of colony-stimulating factor was not included, but this was fully justified. The price year was appropriately reported.

Analysis and results:
The costs and benefits appear to have been appropriately synthesised. The results were clearly presented and an incremental analysis was performed. It was stated that both a probabilistic and a deterministic sensitivity analysis were performed, but the results of the probabilistic analysis were not reported.

Concluding remarks:
The methods seem to have been appropriate, but there were a few limitations. The authors' conclusions appear to be appropriate for their setting.
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