Modeling the cost effectiveness of secondary febrile neutropenia prophylaxis during standard-dose chemotherapy
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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 aim was to assess the cost-effectiveness of secondary infection prophylaxis in small-cell lung cancer patients at risk of febrile neutropenia. The authors concluded that antibiotics plus granulocyte colony-stimulating factor and a sequential strategy were less cost-effective than antibiotics alone. The methodology was appropriate and transparently reported. The conclusions reached by the authors reflect the scope of their analysis.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The aim was to assess the cost-effectiveness of secondary infection prophylaxis in small-cell lung cancer patients at risk of febrile neutropenia.

Interventions
The study considered three secondary prophylactic strategies: antibiotics; antibiotics plus granulocyte colony-stimulating factor (G-CSF); and antibiotics after the first episode of febrile neutropenia, then antibiotics plus G-CSF after the second episode of febrile neutropenia (sequential).

Location/setting
Netherlands/secondary care.

Methods
Analytical approach:
A Markov model with a cycle length of three weeks was used to run two simulations, one with costs as the outcome and the other with cost-effectiveness as the outcome. The time horizon was not reported. The authors stated that the perspective was that of the health care payer.

Effectiveness data:
The clinical parameters were mainly from a phase III randomised controlled trial (RCT), with 85 patients in the antibiotics group and 90 in the antibiotics plus G-CSF group. These patients were treated with five cycles of chemotherapy every three weeks and received primary prophylaxis with antibiotics or with antibiotics plus G-CSF. The main estimates were the incidences of febrile neutropenia. The clinical data were used to estimate the transition probabilities for the model.

Monetary benefit and utility valuations:
None.

Measure of benefit:
The benefit measure was febrile neutropenia-free cycles.

Cost data:
The cost categories included the costs of hospitalisation; visits to the general practitioner, emergency room, or out-patient department; therapeutic antibiotics; laboratory investigations; cultures; and radiologic procedures. The resource
use data were collected during the RCT. Discounting was not relevant, as the costs were likely to be incurred within a time frame of less than one year. All costs were expressed in Euros (EUR).

Analysis of uncertainty:
Probabilistic sensitivity analysis was conducted to assess the parameter uncertainty. The impact of variations in the probabilities of developing febrile neutropenia, the febrile neutropenia recurrence rate, and the febrile neutropenia-related costs were tested in the deterministic sensitivity analysis.

Results
The estimated mean febrile neutropenia-free cycles were 3.81 for antibiotics, 3.83 for antibiotics plus G-CSF, and 3.70 for sequential prophylaxis.

The mean total costs per patient, in the simulation for costs, were EUR 4,496 (95% CI 3,637 to 5,436) for antibiotics; EUR 8,998 (95% CI 7,608 to 10,467) for antibiotics plus G-CSF; and EUR 5,970 (95% CI 4,867 to 7,254) for sequential prophylaxis.

The mean total costs per patient, in the simulation for cost-effectiveness, were EUR 4,745 for antibiotics, EUR 10,567 for antibiotics plus G-CSF, and EUR 6,901 for sequential prophylaxis.

The incremental cost-effectiveness ratio was EUR 343,110 per febrile neutropenia-free cycle for antibiotics plus G-CSF over antibiotics. Compared with antibiotics, the sequential strategy was dominated as it was less effective and more expensive.

In the sensitivity analysis, the cost-effectiveness was sensitive to the main input parameters, such as the probability of developing febrile neutropenia, the febrile neutropenia recurrence rate, and the febrile neutropenia-related costs.

Authors' conclusions
The authors concluded that antibiotics plus G-CSF and the sequential strategy were less cost-effective than antibiotics alone. They recommended research comparing secondary prophylaxis with placebo.

CRD commentary
Interventions:
The authors provided details for the interventions compared and a justification was given for using secondary infection prophylaxis with antibiotics as the comparator.

Effectiveness/benefits:
The use of a phase III RCT as the source for the clinical evidence was appropriate. The trial was described in detail and was of good quality. It was unclear whether this was the only comparative evidence available, as the authors did not report whether or not a systematic review was conducted to find the available data. This use of one trial, if other relevant evidence was available, could be considered a weakness of the study. The measure of health outcome, febrile neutropenia-free cycles, was derived from the RCT and you should consider if this adequately captures the health outcomes of the intervention.

Costs:
All those costs relevant to the perspective appear to have been considered. The resource use data were collected alongside the clinical trial. The sources for the cost data were unclear, but they appear to have been the actual consumption costs for patients participating in the RCT. The cost analysis appears to have been conducted using appropriate methods. The costs were reported at aggregate level, which makes the results less generalisable. The price year was not reported, making reflation exercises difficult.

Analysis and results:
The model structure was presented in a diagram and was well reported. More details of the model were accessible online. A synthesis of the costs and benefits was appropriately carried out. The parameter uncertainty was assessed through probabilistic and deterministic sensitivity analyses. Issues of generalisability to other settings were addressed in
the sensitivity analyses. The authors compared their results with those from other studies.

Concluding remarks:
The methodology was appropriate and transparently reported. The conclusions reached by the authors reflect the scope of their analysis.

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