Cost-effectiveness of primary versus secondary prophylaxis with pegfilgrastim in women with early-stage breast cancer receiving 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
This study evaluated the incremental cost-effectiveness of pegfilgrastim as primary versus secondary prophylaxis in women with early-stage breast cancer, who were receiving myelosuppressive chemotherapy and had a 20% or higher risk of febrile neutropenia. The authors concluded that the cost-effectiveness of primary prophylaxis with pegfilgrastim might be equivalent or superior to other usual supportive care interventions, for women with breast cancer. There were some limitations to the study, and the results and the authors' conclusions should be considered with caution.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The aim was to determine the incremental cost-effectiveness of the granulocyte-colony stimulating factor (G-CSF) pegfilgrastim in primary versus secondary prophylaxis for women with early-stage breast cancer who were receiving myelosuppressive chemotherapy and had a 20% or higher risk of febrile neutropenia.

Interventions
Primary pegfilgrastim was started in cycle one and continued in subsequent cycles of chemotherapy, while secondary pegfilgrastim was given only after an febrile neutropenia event.

Location/setting
USA/secondary care.

Methods
Analytical approach:
The analysis used a decision tree, to model the incidence of febrile neutropenia and the risk of death, and a Markov model, for the ongoing risk of death from breast cancer and other causes. A lifetime horizon was used and the authors stated that a health payer’s perspective was used.

Effectiveness data:
The evidence came from selected studies and the main outcomes were the incidence of febrile neutropenia and the deaths related to it.

Monetary benefit and utility valuations:
The utility values, for the health states, and their ranges were obtained from the literature.

Measure of benefit:
Life-years gained (LYG) and quality-adjusted life-years (QALYs) were the summary measures of benefit. Febrile neutropenia events avoided were also reported, in one scenario analysis. Future benefits were discounted at an annual rate of 3%.

Cost data:
The cost categories included pegfilgrastim, drug administration, initial and repeat febrile neutropenia hospitalisations, and subsequent medical costs related to febrile neutropenia. Chemotherapy costs were assumed to be equal and were
not included. All costs were reported in US dollars ($) and adjusted to 2006 prices, where necessary, using the medical services component of the consumer price index. The sources for the cost data were local and some assumptions were made for in-patient physicians’ fees and out-patient follow-up costs.

Analysis of uncertainty:
Two main scenarios were analysed. In scenario one, it was assumed that the G-CSF had no effect on mortality related to febrile neutropenia and the costs per febrile neutropenia event avoided were reported. In scenario two, an effect on mortality was assumed and the costs per LYG and per QALY were reported. One-way sensitivity analysis was performed, using scenario two and varying the key parameters. A structural sensitivity analysis was performed, by modifying the model and evaluating the probabilities that patients received 85% or more of the adequate dose of chemotherapy and their subsequent impact on mortality, using extrapolated data from the literature. Probabilistic sensitivity analysis was performed.

Results
In scenario two, including mortality benefits, primary prophylaxis was associated with 15.622 LYG, 14.487 QALYs, and a cost of $5,088. Secondary prophylaxis was associated with 15.701 LYG, 14.563 QALYs, and a cost of $13,791.

The incremental cost-effectiveness ratios for primary prophylaxis compared with secondary prophylaxis were $110,000 per LYG (95% CI 84,000 to 136,000) or $116,000 per QALY gained (95% CI 97,000 to 135,000).

These results were most sensitive to changes in the mortality associated with febrile neutropenia cases, the relative risk reduction of febrile neutropenia, the age at breast cancer diagnosis, the baseline risk of febrile neutropenia without primary G-CSF prophylaxis, and the pegfilgrastim cost. The probability that pegfilgrastim primary prophylaxis would be considered cost-effective was 12% at a willingness-to-pay of $50,000 per QALY gained and 40% at $100,000 per QALY gained.

Authors’ conclusions
The authors concluded that, compared with secondary prophylaxis, the cost-effectiveness of primary prophylaxis using pegfilgrastim was less favourable than many health care interventions, but might be equivalent or superior to other commonly used supportive care interventions, for women with breast cancer. They also stated that further assessment of the impact of a G-CSF on the short- and long-term survival of these women was needed to substantiate these findings.

CRD commentary
Interventions:
The dosages of the interventions were not described. The authors provided a justification for only considering pegfilgrastim and not other G-CSFs that were recommended by guidelines, namely filgrastim and sargramostim. It would have been useful to have compared pegfilgrastim with no G-CSF and you should consider if all the relevant options were included because this might affect the cost-effectiveness of pegfilgrastim as primary or secondary prophylaxis.

Effectiveness/benefits:
It was not clear how the sources for the clinical data and the utility data were selected. No search strategy and no inclusion criteria were reported. The authors provided references for the sources of utilities, but did not report their methods.

Costs:
The cost categories were relevant to the selected perspective, which was that of a third-party payer (health payer). The chemotherapy costs were assumed to be equal and were not included, but if pegfilgrastim reduced the incidence of febrile neutropenia it might be expected to increase the number of people who received more chemotherapy, which would have had cost implications. As the chemotherapy costs were not included, all costs were incurred within one year and discounting was not performed. Some of the cost estimates (in-patient physician fees and out-patient costs) were based on data from patients with other diseases, due to a lack of evidence in the literature.

Analysis and results:
The base-case scenario assumed a mortality benefit, from primary prophylaxis with a G-CSF, which was not clearly substantiated by the evidence. The incremental cost-effectiveness analysis was appropriately completed. The authors recommended that further assessment of the direct impact of a G-CSF on mortality was needed.

Concluding remarks:
There were some limitations to the study, which mean that the results and the authors’ conclusions should be considered with caution.

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