Cost-effectiveness of granulocyte colony-stimulating factor prophylaxis for febrile neutropenia in breast cancer in the United Kingdom
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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 study assessed the cost-effectiveness of granulocyte colony-stimulating factors for the prevention of febrile neutropenia after chemotherapy for breast cancer. The authors concluded that pegfilgrastim was the most cost-effective treatment, but was dependent on patient febrile neutropenia risk levels. The quality of the study methods was adequate; both methods and results were reported adequately. Given the scope of the study, the authors’ conclusions appear to be appropriate.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of granulocyte colony-stimulating factors for the prevention of febrile neutropenia after chemotherapy.

Interventions
Seven strategies of prophylaxis were evaluated for breast cancer patients undergoing chemotherapy. Three different granulocyte colony-stimulating factors (pegfilgrastim, filgrastim, and lenograstim) were evaluated for primary prophylaxis (in all cycles of treatment) and secondary prophylaxis (in all remaining cycles of treatment after an episode of febrile neutropenia) compared with no prophylaxis. Six and 11 days of treatment were investigated for filgrastim and lenograstim. Pegfilgrastim involved a single treatment.

Location/setting
UK/Inpatient secondary care.

Methods
Analytical approach:
A mathematical model was constructed to estimate the costs and outcomes associated with the seven interventions. The time horizon was the lifetime of the patient. The authors reported that the perspective of the UK NHS was adopted.

Effectiveness data:
Clinical and effectiveness data were derived from published studies, reports and national statistics. The main measure of effectiveness used in the model was the efficacy of the three granulocyte colony-stimulating factors in reducing febrile neutropenia risk. The authors undertook a full systematic review of the literature, with the results of included trials combined using meta-analyses for each granulocyte colony-stimulating factor prophylaxis compared with no primary granulocyte colony-stimulating factor prophylaxis. The systematic review was an update of an existing meta-analysis (Kuderer, et al. 2007, see 'Other Publications of Related Interest' below for bibliographic details). Analyses were conducted for a mean baseline febrile neutropenia risk of 24%. Additional analyses were conducted for other febrile neutropenia risk levels.

Monetary benefit and utility valuations:
Utility values were dependent on health state (febrile neutropenia or receiving chemotherapy for breast cancer) and age. EQ-5D (European Quality of life) utility estimates were used and were taken from published studies, supplemented with the authors’ own assumptions.
Measure of benefit:
Quality-adjusted life-years (QALYs) were the measure of benefit. They were discounted at an annual rate of 3.5%.

Cost data:
The direct costs included: granulocyte colony-stimulating factor prophylaxis; administration of granulocyte colony-stimulating factor injections; chemotherapy; intravenous antibiotics; daily investigations; febrile neutropenia investigations; and hospitalisation. Only costs incurred during the time the patient was on chemotherapy were included. Costs and resource use were mainly from UK data sources. All costs were reported in UK £. Future costs were discounted using an annual rate of 3.5%. The price year was not explicitly reported.

Analysis of uncertainty:
One-way and two-way sensitivity analyses were undertaken. Probabilistic sensitivity analyses were run using 10,000 sets of parameters sampled independently from probability distributions around each model parameter. Distributions were derived from published sources (where available) or were chosen to fit published 95% confidence intervals. The results were presented using a tornado diagram and cost-effectiveness acceptability curves.

Results
The results were all based on a mean baseline febrile neutropenia risk of 24% for a patient receiving one of the granulocyte colony-stimulating factor strategies along with chemotherapy.

For no granulocyte colony-stimulating factor prophylaxis, the QALYs were 10.060 and the cost per patient was £8,282.

For primary prophylaxis with lenograstim, the QALYs were 10.136 for six and 11 days of treatment. The cost per patient was £12,637 for six days and £16,607 for 11 days.

For secondary prophylaxis with lenograstim, the QALYs were 10.083 for six 11 days of treatment. The cost per patient was £8,744 for six days and £9,250 for 11 days.

For primary prophylaxis with filgrastim, the QALYs were 10.138 for six and 11 days of treatment. The cost per patient was £12,147 for six days and £15,715 for 11 days.

For secondary prophylaxis with filgrastim, the QALYs were 10.084 for six and 11 days of treatment. The cost per patient was £8,679 for six days of treatment and £9,134 for 11 days.

For primary prophylaxis with pegfilgrastim, the QALYs were 10.188 and the cost per patient was £11,841.

For secondary prophylaxis with pegfilgrastim, the QALYs were 10.103 and the cost per patient was £8,556.

Costs and outcomes were combined using an incremental cost-utility ratio (the additional cost per QALY gained). Primary and secondary prophylaxis with lenograstim or filgrastim were dominated by other interventions as they were both more costly and less effective. When compared with no granulocyte colony-stimulating factor prophylaxis, the incremental cost per QALY gained of secondary prophylaxis with pegfilgrastim was £6,500. When compared with secondary prophylaxis with pegfilgrastim, the incremental cost per QALY gained of primary prophylaxis with pegfilgrastim was £38,482.

The results were highly sensitive to baseline febrile neutropenia risk. At a willingness to pay threshold of £20,000 per QALY gained, secondary prophylaxis with pegfilgrastim was most cost-effective at a febrile neutropenia risk level from 11% to 37%. For patients with higher febrile neutropenia risk levels, primary prophylaxis became the most cost-effective.

Authors' conclusions
The authors concluded that pegfilgrastim was the most cost-effective granulocyte colony-stimulating factor treatment, but was dependent on patient febrile neutropenia risk levels.

CRD commentary
Interventions:
The interventions were reported adequately. The rationale for their selection was clear, as the proposed prophylaxis granulocyte colony-stimulating factor strategies were compared with no prophylaxis. No prophylaxis was likely to have been a valid comparator for other health care systems.

Effectiveness/benefits:
Clinical and effectiveness data were mainly from published studies. The main measure of effectiveness (granulocyte colony-stimulating factor efficacy) was from a systematic review of the literature, which updated the results from a published review. All identified trials were combined using meta-analyses techniques. The authors provided only brief details of the systematic literature search, but referred to the earlier published review and online appendix for more details of the included trials. As a systematic review was conducted, it was highly likely that all relevant major information on effectiveness was included in the model. QALYs were an appropriate benefit measure for capturing the impact of the interventions on the patients’ health and to allow cross-disease comparisons.

Costs:
The perspective adopted was explicitly reported to be that of the UK NHS. All the relevant costs for this perspective appeared to be included in the analysis. The sources from which unit costs and resource use were derived were adequately reported. The unit costs and resource use were generally reported separately, which enhanced the study transparency. The time horizon, discount rate and currency used were reported. However, the price year was not reported, which may hamper any future inflationary exercises.

Analysis and results:
An incremental approach was appropriately used to synthesise the costs and benefits of the alternative strategies. Adequate details of the decision analytic mathematical model structure were provided including a diagram. The results were clearly reported. Uncertainty was exhaustively assessed using one-way, two-way and probabilistic sensitivity analyses. As a main limitation to their study, the authors acknowledged that they had to make a number of assumptions due to lack of data available (such as UK specific data).

Concluding remarks:
The quality of the study methods was adequate; both methods and results were reported adequately. Given the scope of the study, the authors’ conclusions appear to be appropriate.

Funding
The study research was funded by Amgen Ltd. The production of the article was supported by a research grant from Amgen (EUROPE) GmbH.

Bibliographic details

PubMedID
21669371

DOI
10.1016/j.jval.2010.10.037

Original Paper URL
http://www.valueinhealthjournal.com/article/S1098-3015(10)00056-2/abstract

Other publications of related interest
Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Breast Neoplasms /drug therapy /economics /epidemiology; Cost-Benefit Analysis /economics; Female; Fever /economics /epidemiology /prevention & control; Granulocyte Colony-Stimulating Factor /administration & dosage /economics; Great Britain /epidemiology; Humans; Middle Aged; Models, Economic; Neutropenia /economics /epidemiology /prevention & control

Accession Number
22011001630

Date bibliographic record published
12/04/2012

Date abstract record published
28/05/2012