Universal prophylaxis is cost effective in cytomegalovirus serology-positive kidney transplant patients

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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 examined the cost-effectiveness of universal prophylaxis versus pre-emptive therapy to manage cytomegalovirus infection in serology-positive kidney transplant patients. The authors concluded that universal prophylaxis was more clinically effective and less expensive than pre-emptive therapy and should be used to prevent cytomegalovirus infection. The data sources were not well described and there were some methodological limitations that might affect the validity of the authors’ conclusions.

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

Study objective
This study examined the cost-effectiveness of universal prophylaxis versus pre-emptive therapy, for the management of cytomegalovirus infection in serology-positive (R+) kidney transplant patients.

Interventions
Universal prophylaxis with valganciclovir (900mg daily for 90 days) was compared against pre-emptive therapy (viraemia polymerase chain reaction testing) for cytomegalovirus in R+ kidney transplant patients.

Location/setting
USA/out-patient.

Methods
Analytical approach:
The analysis was based on a decision-tree model, followed by a Markov chain. A 10-year time horizon was considered. The authors did not explicitly state the perspective adopted.

Effectiveness data:
The clinical data were derived in two ways. The data for universal prophylaxis were from a cohort of all eligible patients identified from March 2002 to December 2007 at the authors’ institution. This included 653 patients who were followed-up until their graft loss and death, or June 2009 (the end of the study). The data for pre-emptive therapy were from six published clinical trials (416 patients) identified by a literature review. The probability of cytomegalovirus infection was the key input of the model.

Monetary benefit and utility valuations:
The utility values were from published sources.

Measure of benefit:
The cases of infections avoided and quality-adjusted life-years (QALYs) were the summary benefit measures.

Cost data:
The economic analysis included both direct and indirect costs. The direct costs were the expenses of prophylaxis, monitoring, diagnosis, and treatment of cytomegalovirus infection during the first year, including valganciclovir and polymerase chain reaction test to monitor and diagnose the virus, physician and nurse fees, filgrastim administration,
hospital care, and the opportunity costs of working days lost. The indirect costs were the expenses of maintaining a patient with a functioning kidney graft, a failing kidney graft, while on dialysis, and subsequently having a re-transplant. The unit costs and resource quantities were from published sources and from the authors’ institution. The costs were in US dollars ($) and were discounted at an annual rate of 5%. The price year was 2008.

Analysis of uncertainty:
One- and two-way sensitivity analyses were carried out focusing on changes in the incidence of cytomegalovirus infection with universal prophylaxis.

Results
The total costs were $407,754 (direct $7,963 and indirect $399,792) with universal prophylaxis and $413,599 (direct $6,499 and indirect $407,100) with pre-emptive therapy. The rate of infection avoided was 0.95 with universal prophylaxis and 0.45 with pre-emptive therapy. The QALYs gained were 5.978 with prophylaxis and 5.769 with pre-emptive therapy.

Considering the direct costs, over the first year, the incremental cost per infection avoided with prophylaxis over pre-emptive therapy was $2,928. Considering all costs, over 10 years, prophylaxis was dominant, as it was less expensive and more effective than pre-emptive therapy.

Universal prophylaxis remained dominant as long as the incidence of cytomegalovirus infection with universal prophylaxis was less than 20%; the incremental cost per QALY gained was acceptable ($71,000) even at a rate of 30%. In general, the dominance of universal prophylaxis was robust to the variations in the two-way sensitivity analyses.

Authors’ conclusions
The authors concluded that universal prophylaxis was more clinically effective and less expensive than pre-emptive therapy and should be used to prevent cytomegalovirus infection.

CRD commentary
Interventions:
The selection of the comparators was appropriate; the authors noted that the two interventions were equally recommended for R+ kidney transplant recipients.

Effectiveness/benefits:
Two separate cohorts of patients were used to provide evidence for the two interventions. The authors did not mention the comparability of these two cohorts, which was critical to ensure the validity of the comparison. Statistical analyses were reported to assess the baseline comparability of patients with and without cytomegalovirus infection, within the universal prophylaxis group only, and to identify the risk factors for cytomegalovirus infection. The methods and conduct of the literature review performed to identify the sources of data on pre-emptive therapy were not reported, but the use of clinical trials should ensure high internal validity. These issues might affect the validity of the clinical inputs. Two benefit measures were used and QALYs capture the impact of the intervention on both survival and quality of life. No information on the utility valuations was given. The authors stated that the benefits of the interventions were not discounted as the rates of graft loss and death were assumed to be constant over the 10 years.

Costs:
A broad perspective was adopted to include both the direct medical and indirect costs. These were presented as key categories, but the unit costs and resource quantities were not presented for all items. The data sources were not clearly described. In general, the economic data were not transparently presented. The price year and discounting were reported.

Analysis and results:
An appropriate incremental analysis was used to synthesise the costs and benefits, which were clearly presented for both strategies. The uncertainty was partly investigated, by varying the rates of cytomegalovirus infection and disease. Variations in the costs and other clinical inputs were not assessed. The study appears to have been US-specific and might be difficult to transfer to other settings, particularly as few details of the costs were reported, but more
information might be available in the supplementary material. The main issue of the analysis was the potential differences between the two cohort of patients for the universal prophylaxis and for the pre-emptive therapy.

Concluding remarks:
The data sources were not well described and there were some methodological limitations that might affect the validity of the authors’ conclusions.

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