Prolonged prophylaxis with valganciclovir is cost effective in reducing posttransplant cytomegalovirus disease within the United States

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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 prolonged prophylaxis (200 days) with valganciclovir compared with 100-day prophylaxis to prevent cytomegalovirus disease in high-risk seronegative kidney transplant recipients from seropositive donors. The authors concluded that prolonged prophylaxis reduced the incidence of cytomegalovirus-associated events and was cost-effective. The cost-effectiveness framework was conventional and the clinical and economic sources were valid. The authors’ conclusions seem robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to examine the cost-effectiveness of prolonged prophylaxis (200 days) with valganciclovir compared with 100-day prophylaxis to prevent cytomegalovirus disease in high-risk seronegative kidney transplant recipients from seropositive donors.

Interventions
Prolonged prophylaxis with valganciclovir (200-day) was compared with 100-day prophylaxis.

Location/setting
USA/secondary care.

Methods
Analytical approach:
The analysis was based on a cohort Markov model with two time horizons, five and 10 years. The authors stated the study perspective to be that of the health care payer.

Effectiveness data:
The clinical data appear to have been derived from a selection of relevant studies. Key evidence on the short-term efficacy and safety profile of prophylaxis and the baseline patients’ population were retrieved from the Improved Protection Against cytomegalovirus in Transplant (IMPACT) study, which was a prospective, randomised controlled trial that followed patients for one year (Humar, et al. 2010, see ‘Other Publications of Related Interest’ below for bibliographic details). This study was used to estimate the rate of cytomegalovirus in the first year after prophylaxis, which was the key input of the model. A systematic literature review was undertaken to identify the data beyond the first year of prophylaxis. The rate of cytomegalovirus in subsequent years was derived from a retrospective study conducted in the USA.

Monetary benefit and utility valuations:
The utility values were from the literature review, which identified several sources. The estimates used were those from a published study that used the time trade-off instrument.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and were discounted at an annual rate of 3%.
Cost data:
The economic analysis included the costs of prophylaxis, cytomegalovirus disease (in-patient treatment and drug therapy), post-cytomegalovirus (functioning graft), acute rejection, graft failure, and dialysis. All economic data were derived from two published economic evaluations conducted in the USA. The costs were in US dollars ($), a 3% annual discount rate was applied, and the price year was 2009.

Analysis of uncertainty:
One-way sensitivity analyses were carried out to assess how robust the base-case findings were to ±10% changes in the model inputs. Alternative discount rates (zero and 5%) were considered.

Results
In a hypothetical cohort of 10,000 patients, the projected costs over five years were $624,433,251 with 100-day prophylaxis and $635,849,658 with 200-day prophylaxis. The benefits were 29,581 QALYs with 100-day prophylaxis and 30,349 QALYs with 200-day prophylaxis. The incremental cost per QALY gained was $14,859.

In a hypothetical cohort of 10,000 patients, the projected costs over 10 years were $1,065,150,672 with 100-day prophylaxis and $1,063,405,609 with 200-day prophylaxis. The benefits were 47,639.9 QALYs with 100-day prophylaxis and 50,020.3 QALYs with 200-day prophylaxis. The 200-day prophylaxis was dominant as it was more effective and less expensive.

The highest incremental ratio remained well below the threshold of $50,000 per QALY. The base-case findings were robust to variations in the model inputs.

Authors' conclusions
The authors concluded that prolonged prophylaxis (200 days) with valganciclovir reduced the incidence of cytomegalovirus-associated events in high-risk kidney transplant patients and was a cost-effective strategy.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear. The authors stated that oral valganciclovir is the most commonly used preventive treatment for this patient population because of its convenient dosing scheme and administration.

Effectiveness/benefits:
The clinical evidence for the short-term horizon was based on a recent clinical trial, which provided up-to-date inputs for the two prophylactic strategies; the details of this trial were presented in the paper. Supplementary data were based on a literature review, but its methods and conduct were not reported and the quality of this evidence cannot be assessed. Inputs were derived from multiple published sources, but to reduce heterogeneity the authors stated that these studies closely matched the characteristics of the baseline population of the IMPACT trial. The use of an observational study to extrapolate the short-term data to the long-term was appropriate. The utility values were from a 1996 study, which was still considered a cornerstone for the assessment of health-related quality of life. This study used a valid instrument to elicit the preferences and covered the time from before transplant to 24 months after. QALYs were an appropriate benefit measure given the impact of the disease on survival and quality of life. They are comparable with the benefits of other health care interventions.

Costs:
The cost categories were consistent with the perspective, which was restricted to the direct medical costs. A breakdown of cost items was not given. To adopt a conservative approach, the cost of cytomegalovirus disease maintenance therapy (secondary prophylaxis) was not included. Details of the unit costs and quantities of resources used were not reported. No information on data sources was provided, except that the data were from published economic evaluations conducted in the USA and they should have been representative of the authors’ context. The price year and the use of discounting were clearly reported.

Analysis and results:
The study results were clearly presented for both time horizons. An incremental approach was appropriately used to synthesise the costs and benefits of the two approaches. The analysis of uncertainty was restricted to a deterministic approach; the findings confirmed that the base-case results were robust. A more comprehensive analysis would have been interesting as the model parameters were only varied by 10% and using a univariate approach. The authors stated that a conservative approach against prolonged prophylaxis was used when assumptions were needed. The analysis appears to have been specific to the US context and cannot be easily transferred to other settings.

Concluding remarks:
The study was based on a conventional cost-effectiveness framework and on valid clinical and economic sources. The authors' conclusions seem robust.

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**Other publications of related interest**

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