A comparative randomised study of valacyclovir vs. oral ganciclovir for cytomegalovirus prophylaxis in renal transplant recipients

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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.

Health technology
The study examined the use of oral valacyclovir (2 g every 6 hours) versus oral ganciclovir (1 g every 8 hours) for cytomegalovirus (CMV) prophylaxis in renal transplant patients. The drug dosage was adjusted for renal function and was given for the first 3 months after transplantation.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised male and female patients older than 14 years who received renal transplantation, from a living or deceased donor, in Athens, Greece. The CMV serological status of the donor or recipient was not relevant. Patients with active herpes virus infection were excluded, as were those who had received other antiviral agents in the 2 weeks before transplantation.

Setting
The setting was not specified, but it was likely to have been secondary or tertiary care. The economic evaluation was carried out in Athens, Greece.

Dates to which data relate
The effectiveness evidence and resource use data were collected between April 1999 and September 2000. The price year was not specified, but the prices of the drugs appear to have been current when the manuscript was written (2004).

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was estimated and was based on the same sample of patients as that used in the effectiveness study. However, it was unclear if the costing was performed prospectively or retrospectively.

Study sample
Power calculations were not used to determine the sample size. The sample consisted of all patients undergoing renal transplantation at the study centre who met entry criteria during the study period. Of the 100 patients undergoing renal
transplant during the study period, 83 fulfilled the inclusion criteria and completed the trial. Forty-three patients received valacyclovir and 40 received oral ganciclovir.

**Study design**
This was an open, prospective, randomised study that was conducted at a single centre. The patients were followed up for 6 months after transplantation. Follow-up was complete for all of the patients included in the study.

**Analysis of effectiveness**
The analysis of the clinical study was conducted on an intention to treat basis. The primary outcomes were occurrence of CMV infection and/or disease during the first 6 months following transplantation, and drug-related adverse events during prophylaxis. The secondary end points were the frequency of acute graft rejection, the occurrence of other viral and bacterial infections, and renal function (serum creatinine levels). The groups were shown to be comparable at baseline.

**Effectiveness results**
CMV infection was observed in only one patient belonging to the ganciclovir group.

Compliance was 100% in both groups.

No difference was observed between the two groups with respect to the detection of CMV DNA, virus infections other than CMV, acute rejection episodes, or serum creatinine levels at 3 and 6 months following transplantation.

An increased number of bacterial infections was noted in the ganciclovir group compared with the valacyclovir group (90% versus 53.5%; p=0.003), and in urinary tract infections (53% versus 23%; p<0.02).

No adverse reactions to either treatment were reported.

**Clinical conclusions**
Overall, both valacyclovir and oral ganciclovir were found to be effective and safe for CMV prophylaxis in renal transplant recipients.

**Measure of benefits used in the economic analysis**
There was no summary measure of benefit so, in effect, a cost-consequences analysis was performed.

**Direct costs**
Discounting was not performed, nor was it relevant since the costs were incurred during less than 2 years. The estimations of the quantities and costs were based on actual data. The mean quantity of drugs use per patient in each group was used to calculate the total cost of treatment for 3 months. The unit costs were reported separately. The cost of the drugs was based on the price of drugs as marketed in Greece. The price year was not reported, but it would appear to relate to the prices prevalent when the paper was written (2004). Protocol-driven costs were not included.

**Statistical analysis of costs**
A statistical analysis of the costs was not performed.

**Indirect Costs**
The indirect costs were not included.
Currency
Euros (EUR).

Sensitivity analysis
A sensitivity analysis was not performed.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
Valacyclovir prophylaxis was estimated to cost EUR 1,721 over 3 months and ganciclovir was estimated to cost EUR 1,466.

The authors stated that all other costs were similar in the two groups.

Synthesis of costs and benefits
The costs and benefits were not combined because of the cost-consequences approach adopted.

Authors' conclusions
The estimated cost of valacyclovir prophylaxis was 20% higher than that for ganciclovir. The drugs had comparable efficacy and safety.

CRD COMMENTARY - Selection of comparators
The rational for the choice of the comparator was clear. It represented standard practice in the authors' setting. You should decide if it represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness was based on a randomised, prospective study, but it was unclear whether the sample size was large enough as no power calculations were reported. The single-centre nature and open design of the study may also restrict its internal and external validity.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis so, in effect, a cost-consequences analysis was conducted. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The perspective adopted in the study was not explicitly reported, but it appears to have been that of the Greek health care system. The indirect costs were not included. In the context of long-term care of transplant patients, a societal perspective would, perhaps, have been more informative. With the exception of the price of the drugs and the mean cost of hospitalisation, details of the analysis of resources used and unit costs were not reported. This means that it would be difficult to replicate the study in other settings. Discounting was not performed, but it was not relevant as the costs were incurred during less than 1 year.

Other issues
The authors made several comparisons of their findings with those from other studies. However, the issue of
generalisability to other settings was not explicitly addressed.

**Implications of the study**

The authors suggested that further investigations are needed to define the optimal prophylactic regimen for this patient population. They also highlighted the fact that prophylactic use of ganciclovir could allow the development of resistance to this drug, which is usually used to treat CMV infection. They implied that the probability of developing resistance needs to be investigated before decisions regarding prophylactic regimens are taken.

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