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A decision-analytic economic evaluation of valaciclovir prophylaxis for the prevention of cytomegalovirus infection and disease in renal transplantation

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Abstract: Objective: This analysis evaluates the cost-effectiveness of valaciclovir prophylaxis using clinically and economically important health outcomes including graft failure, life-years, and quality-adjusted life-years (QALYs).
Methods: A Markov model was developed using a randomized, placebo-controlled trial of valaciclovir prophylaxis, together with a published epidemiological study and national renal transplant registry data. The model's population was stratified into two risk groups by donor/recipient cytomegalovirus (CMV) serostatus at transplantation: donor-positive/recipient-negative (D + R−) and recipient-positive (R +) patients. The model estimated costs and health outcomes over a 30-yr period from the perspective of Australian health care providers.
Results: The total health care cost was $3619 lower for D + R− patients receiving valaciclovir prophylaxis compared with those not receiving prophylaxis. D + R− patients receiving valaciclovir gained an extra 0.33 yr of life and 0.27 QALYs. R + patients receiving valaciclovir prophylaxis gained an extra 0.07 yr of life and 0.05 QALYs, with an incremental cost of $914. This equates to $17 127 per QALY gained, which is highly cost-effective compared with other drugs and health interventions.
Conclusions: Valaciclovir for the prophylaxis of CMV disease in renal transplant recipients is a cost-effective intervention, significantly reducing the burden of CMV disease to patients and health care providers.

Dominic P Tilden[a], Jeremy Chapman[b], Peter J Davey[c], Michaela L Solly[d] and Steven Crowley[e]

[a] M-TAG, London, UK, [b] Renal Unit, Westmead Hospital, University of Sydney, NSW, [c] M-TAG, Sydney, NSW, [d] GlaxoSmithKline Australia, Melbourne, Victoria, and [e] Janssen Cilag, Sydney, NSW, Australia

Key words: cost effectiveness – cytomegalovirus – renal transplantation – utility theory – valaciclovir

Corresponding author: Dominic P. Tilden, M-TAG Limited, Level 3, Lee House, 109 Hammersmith Road, Hammersmith, London, W14 0QH, UK.
Tel.: +44 (0)207 603 1671;
Fax: +44 (0)207 603 1744;
e-mail: dtilden@m-tag.net

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Graft loss in renal transplantation, caused by death or acute or chronic graft rejection, is costly to patients and health care providers, and may be preventable. This evaluation used the results of a large randomized controlled trial (1), together with other data sources, to estimate the benefits, in terms of reduced health care costs and better health outcomes, of valaciclovir prophylaxis for the prevention of cytomegalovirus (CMV) disease and acute graft rejection.

Several authors have found a significant relationship between CMV disease and acute graft rejection. Lewis et al. reported a higher rejection rate in the first year post-transplant in CMV-infected renal transplant recipients compared with non-infected controls (48% vs. 25%, $p < 0.001$) (2). This finding was confirmed in a large prospective study by Pouteil-Noble et al. (3). Renal transplant recipients with CMV infection had more than four times the risk of developing acute

rejection (AR) than those without (45% vs. 11%, $p < 0.0001$).

A number of different factors are believed to influence the development of CMV disease after transplantation (4, 5). In this economic evaluation, the serological status of donors and recipients with respect to CMV Immunoglobulin G (IgG) at transplantation (donor/recipient serostatus) was considered the primary risk factor.

The presence of CMV disease increases the total cost of renal transplantation as well as reducing its effectiveness, thus dramatically diminishing the cost-effectiveness of renal transplants. In a case-control study of the cost impacts of CMV disease in renal transplant recipients, McCarthy et al. estimated that institutional health care costs were 2.5 times higher in patients with CMV disease than in those without (6).

Valaciclovir prophylaxis is one of many possible strategies for management of CMV risk after renal transplantation (7). Other options include oral aciclovir (8), and oral and intravenous ganciclovir (9–12). However, prior to the introduction of valaciclovir, no other antiviral agent was available through Australia's Schedule of Pharmaceutical Benefits for CMV prophylaxis in renal transplant recipients.

Previous economic evaluations of valaciclovir prophylaxis as a therapeutic strategy to prevent CMV disease in renal transplant recipients have found it effective in decreasing the costs associated with CMV disease. Legendre et al. performed a cost-effectiveness analysis from the perspective of the French health care system, using the trial population reported by Lowance et al. (1). They found the use of valaciclovir prophylaxis resulted in lower total health care costs in donor CMV IgG positive, recipient CMV IgG negative (D+R−) patients during the 6-month period following transplantation (13). Mauskopf et al. modeled different CMV management strategies in D+R− patients. They concluded valaciclovir prophylaxis was associated with a lower incidence of CMV disease at modest incremental cost, compared with pre-emptive or 'wait-and-treat' therapy with intravenous ganciclovir (14).

Unfortunately, neither of these evaluations considered any outcomes of therapy beyond the development of CMV disease. CMV disease is an intermediate outcome of therapy and it is important that more final, patient-relevant outcomes also be considered. Final outcomes of therapy, such as quality-adjusted life-years (QALYs), are useful when assessing cost-effectiveness because they provide a standard unit for measuring benefit, which enables comparisons across a range of therapeutic areas.

It was the aim of this evaluation to use the data collected by Lowance et al. to perform a long-term rigorous economic evaluation of valaciclovir for CMV prophylaxis in renal transplantation (1). The assessment of the cost-effectiveness of valaciclovir prophylaxis relative to no prophylaxis, in both D+R− and R+ patients (R+ patients include both D−R+ and D+R+ patients), inclusive of the longer term costs and the final health outcomes associated with CMV disease and AR, are reported here.

Methods

The comparison

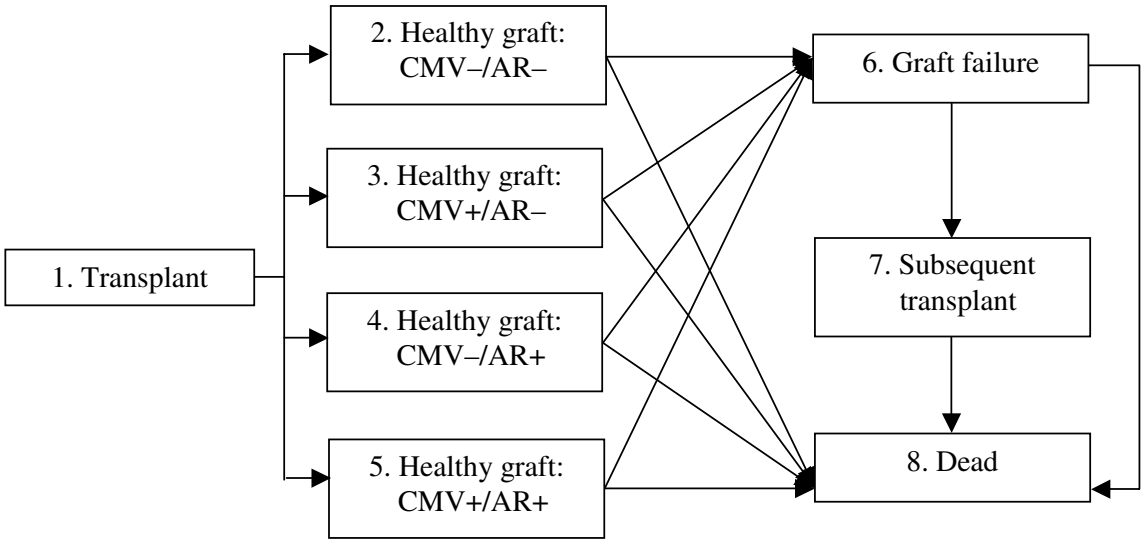
Valaciclovir for CMV prophylaxis was added to Australia's national formulary, the Schedule of Pharmaceutical Benefits, in November 2000. Prior to this, no antiviral agent was available through the schedule for the prophylaxis of CMV infection and disease following renal transplantation. Therefore, the most appropriate comparator for assessing the relative costs and benefits of valaciclovir prophylaxis in Australia was placebo or no prophylaxis.

The modeled economic evaluation employed a Markov process to compare the costs and health outcomes of valaciclovir prophylaxis with no prophylaxis (placebo). The model was based on the outcomes of Lowance et al.'s multicentre, randomized, double-blind, double-dummy, parallel group trial (1). Patients in the study had a moderate to high risk of CMV infection or disease, based on donor/recipient CMV serostatus. The sample was prospectively stratified into two populations, moderate-risk (R+) patients, and high-risk (D+R−) patients.

A literature search did not identify any further clinical trials comparing valaciclovir prophylaxis and placebo in this indication. Therefore, the Lowance et al. trial comprised the best available evidence with which to form the basis of the economic model. The decision-analytic model was also stratified by donor/recipient CMV serostatus, meaning it was able to estimate the cost-effectiveness of valaciclovir prophylaxis relative to no prophylaxis in each of these important patient populations.

The model's eight health states

In the Markov process, patients progress through eight health states, in 6-month cycles, over a period of 30 yr following transplantation. The probabilities of entering each health state are different for valaciclovir prophylaxis and no prophylaxis and



Health state	Brief description of health state
Transplant	All patients enter the Markov process via this state. They incur valaciclovir and medical resource use costs as observed in the Lowance et al. trial (1) (Table 4). Surviving patients exit this state, depending on trial data, in one of four health states: CMV–/AR–, CMV+/AR–, CMV–/AR+, and CMV+/AR+.
Functioning graft: CMV–/AR–	Patients entering this health state did not develop CMV disease or experience an episode of AR during the clinical trial. Patients in this state are at lowest risk of graft failure (18).
Functioning graft: CMV+/AR–	Patients entering this health state developed CMV disease but did not experience an episode of AR during the clinical trial. Patients in this state are also at lowest risk of graft failure (18).
Functioning graft: CMV–/AR+	Patients entering this health state did not develop CMV disease, but experienced an episode of AR during the clinical trial. Patients in this state are at higher risk of graft failure than patients who have not experienced an AR episode (18).
Functioning graft: CMV+/AR+	Patients entering this health state developed CMV disease and experienced an episode of AR during the clinical trial. Patients in this state are at highest risk of graft failure (18).
Graft failure	In this state patients have experienced graft failure. Patients are dialyzed while awaiting a new transplant. They are at higher risk of death and experience a lower quality of life than patients with a functioning graft. Patients remain in this health state until they receive a subsequent transplant or die.
Subsequent transplant	In this state patients receive a subsequent transplant following graft failure. The model assumes that all subsequent transplants are successful and the patient stays in this health with a functioning graft until death.
Death	Patients entering this state die following transplantation and progression through the model is terminated.

Fig. 1. Possible transitions between health states in the Markov process.

are derived from clinical trial data. Each health state in the modeled evaluation is described in Fig. 1.

To calculate cost-effectiveness using a Markov process, three data items are required for each health state. They are: a cost item, a health outcome item, and a transition probability.

Measuring costs

All costs were measured from the perspective of the health care provider, meaning only direct health care costs were included. A discount rate of 5% per annum was applied to both costs and health outcomes. Discounting converts these data to a present day value, in recognition of the fact that a certain sum of money paid or benefit gained in the future has less value than the same sum today. A rate of 5% is consistent with the requirements of the Australian government (15).

The costs of each health state are presented in Table 1. Direct medical costs for the transplant health state were derived from the Lowance et al. clinical trial (1). The trial recorded medical resource use by patients in each treatment group. Resources used include study drug medication, concomitant medication, hospitalization, physician visits, outpatient services, and laboratory procedures. Total treatment costs were calculated by multiplying the mean medical resource use for each treatment group by the appropriate unit price. Legendre et al. employed this approach with the Lowance et al.

Table 1. Health state treatment costs

Health state	Cost of treatment for 6 months in health state		Source
Transplant	Valaciclovir		Medical resource use trial data on file. Resources include valaciclovir, hospitalization, medical services and concomitant medications (Table 4).
	D+R−	$20 448	
	R+	$18 522	
	Placebo		
	D+R−	$19 199	
	R+	$16 616	
Functioning graft		$2707	Mitchell *et al.* (16)[a]
Graft failure		$13 296	VMDP (99/00)
Subsequent transplant[a,b]		$20 701	AR-DRGs L01A and L01B
Functioning graft (following re-transplant)		$2707	Mitchell *et al.* (16)[a]

[a] Cost adjusted to 2000 prices using Government Final Consumption Expenditure (Hospital and Nursing Home Care) Price Index (July 1999).
[b] This cost is incurred once only.
VMDP, Victorian Maintenance Dialysis Program; AR-DRG, Australian Refined Diagnosis Related Group.

Table 2. Transition probabilities applied to the Markov process

Transition probability	Valaciclovir	Placebo	Source
Probability of death within 6 months of transplant	0.03	0.03	ANZDATA 1999 (19)
Probability of CMV−/AR− after transplant			
D+R− patients	0.667	0.349	Clinical trial data on file (1)
R+ patients	0.721	0.637	(012R+ and 012R−)
Probability of CMV+/AR− after transplant			
D+R− patients	0.088	0.160	Clinical trial data on file (1)
R+ patients	0.000	0.025	(012R+ and 012R−)
Probability of CMV−/AR+ after transplant			
D+R− patients	0.196	0.264	Clinical trial data on file (1)
R+ patients	0.270	0.309	(012R+ and 012R−)
Probability of CMV+/AR+ after transplant			
D+R− patients	0.049	0.226	Clinical trial data on file (1)
R+ patients	0.010	0.029	(012R+ and 012R−)
Probability of graft failure			
0–10 yr	Dependent on CMV/AR status and age of graft (see Fig. 2)		Humar *et al.* (18)
After 10 yr	0.000		Assumption
Probability of death, with functioning graft (6-month period)			
Age 35–44	0.005		
Age 45–54	0.010		
Age 55–64	0.018		
Age 65+	0.038		ANZDATA 1999 (19)
Probability of death, with graft failure			
Age 35–44	0.037		
Age 45–54	0.068		
Age 55–64	0.068		
Age 65+	0.126		ANZDATA 1999 (19)
Probability of re-transplant (following graft failure)	0.061		ANZDATA 1999 (19)

ANZDATA, Australia and New Zealand Dialysis and Transplant Registry.

trial data using French unit prices (13). Australian unit prices were derived from the Schedule of Pharmaceutical Benefits (November 2000), the Medicare Benefits Schedule (November 2000), and the Australian Refined Diagnosis Related Groups version 4 (1997/98 All Hospitals Public Sector).

For health states in which patients have a functioning graft, a cost of $2707 per patient was applied. This cost (adjusted to year 2000) was used by Mitchell et al. and represents the ongoing cost of medical resources used by transplant recipients with a functioning graft (16). This cost is applied irrespective of the patient's CMV/AR status in the model.

A cost of $13 296 was applied to the graft failure health state. This represents the cost of dialysis

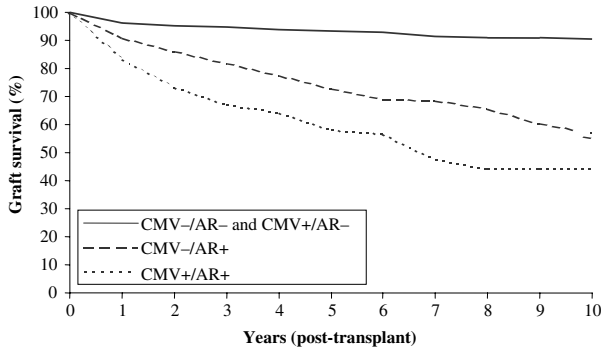


Fig. 2. Transition probability to graft failure by CMV disease and AR status.

over a 6-month period in the Victorian Maintenance Dialysis Program (weighted by the type of dialysis used).

For the subsequent transplant health state, a once-only cost of $20 701 was applied, representing the cost of a renal transplant in Australia (Australian Refined Diagnosis Related Groups version 4).

Measuring health outcomes

Health outcomes were measured as life-years and QALYs gained. For measuring QALYs, utility values were derived for patients with a functioning graft and for those with graft failure. Utility values are a numerical weighting to represent differences in quality of life, and can range from 0 for death to 1 for perfect health. QALYs are the life-years multiplied by the utility value representing the quality of life. For example, a person who lives in a health state with a utility value of 0.5 for 2 yr has gained two life-years but only one QALY (0.5×2).

The utility values used in the modeled economic evaluation were from a quality of life study of 168 renal transplant patients by Laupacis et al. (17). Patients with a functioning graft (health states 1–5, 7) had a utility value of 0.70, while those whose graft had failed (health state 6) and were receiving dialysis had a utility value of 0.57. These values were estimated by Laupacis et al. using the time trade-off technique and correspond with the utility values for patients 18 months after transplant (functioning graft) and immediately before transplant (dialysis).

Estimating transition probabilities

Transition probabilities were estimated from three sources: the clinical trial data (1), a large (n = 1339) study of renal transplant patients examining the relationship between CMV disease, AR, and graft survival over a period of 10 yr (18), and a national renal transplant database (Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) 1999) (19). All transition probabilities used are presented in Table 2.

Transition probabilities from the transplant health state to one of four CMV disease/AR health states (CMV−/AR−, CMV+/AR−, CMV−/AR+, CMV+/AR+) were determined based on the results of the pivotal clinical trial (1). These probabilities, which depend upon the treatment received (valaciclovir prophylaxis or no prophylaxis) and the donor/recipient CMV serostatus (D+R− or R+), were calculated from individual patient data using intention-to-treat principles. The Fisher–Freedman–Halton non-parametric test was used to compare the distribution of the four health states across the two treatment groups and according to donor/recipient CMV serostatus.

The transition probabilities from a functioning graft to graft failure, determined from Humar et al. (18), depend on the patient's CMV/AR status and the age of the graft (Fig. 2). Transition probabilities from Humar et al. were only available for 10 yr following transplantation. After this time, the model assumes that patients are no longer at risk of graft failure.

The probability of death for patients with functioning or failed grafts, was determined from the ANZDATA database (19).

Calculating costs and health outcomes over the period of the model

For the D+R− and R+ patient populations, the Markov process uses the costs, health outcomes and transition probabilities described above, to

Table 3. Trial data applied to the modeled evaluation

	D+R− patients		R+ patients	
CMV disease and AR outcome at 6-month follow-up	Valaciclovir (n = 102) n (%)	Placebo (n = 106) n (%)	Valaciclovir (n = 204) n (%)	Placebo (n = 204) n (%)
CMV−/AR−	68 (67)	37 (35)	147 (72)	130 (64)
CMV+/AR−	9 (9)	17 (16)	0 (0)	5 (2)
CMV−/AR+	20 (20)	28 (26)	55 (27)	63 (31)
CMV+/AR+	5 (5)	24 (23)	2 (1)	6 (3)

calculate the expected total costs, life-years and QALYs accumulated per patient receiving valaciclovir prophylaxis and no prophylaxis over the 30-year post-transplant period. A sensitivity analysis considered the clinical trial efficacy data, the risk of graft failure, hospital and concomitant medication costs during the trial period, the duration of the model, and discounting. These model parameters were chosen for sensitivity analysis in order to assess their importance to the cost-effectiveness results.

Results

CMV disease and AR

Table 3 shows the incidence of CMV disease and AR by treatment group and donor/recipient CMV serostatus, as applied in the economic evaluation. Over the 6-month trial period, the incidence of laboratory-confirmed CMV disease in D+R− patients was significantly lower in the valaciclovir group than in the placebo group (14% vs. 39%, $p < 0.0001$), as was the incidence of laboratory-confirmed AR (25% vs. 49%, $p < 0.001$). In R+ patients, the incidence of CMV disease was also lower in valaciclovir-treated patients (1% vs. 5%, Fisher's exact $p = 0.02$), as too the incidence of AR (28% vs. 34%, $p = 0.20$).

The Fisher–Freedman–Halton non-parametric test shows a significant difference at the 5% significance level in distribution of the four health states across the valaciclovir and placebo groups in both the D+R− patients ($p < 0.0001$) and R+ patients ($p = 0.03$).

These results are similar to those reported by Lowance et al. (1), where Kaplan–Meier survival estimates for CMV disease and AR were reported independently of each other. However, the modeled economic evaluation requires categorical data on the number of patients in each of the four CMV/AR combination health states. These data could only be obtained by analysing individual patient data from the trial database (trial data on file).

Graft failure

The transition probabilities to graft failure according to CMV disease and AR status is presented in Fig. 2 (after 10 yr the risk of graft failure was assumed to be zero for all patients). The risk of graft failure was highest for patients who experienced both CMV disease and AR ($p = 0.0004$). Patients with AR and no CMV disease had the next highest risk of graft failure. Humar et al. found CMV disease did not affect the risk of graft failure in patients without AR ($p =$ not significant). Patients free of AR (with or without CMV) had the lowest risk of graft failure (18).

Costs during the first 6-months post transplant

Table 4 compares the costs of medical resource use during the 6-month post transplant follow-up period of the trial. The cost of valaciclovir prophylaxis, according to the actual amount of medication used during the trial, was $3904 per D+R− patient and $3589 per R+ patient (using the dispensed price of $4.84 per 500 mg valaciclovir tablet; Schedule of Pharmaceutical Benefits November 2000).

The costs of other medical resources used by both D+R− and R+ patients during the 6-month follow-up period of the trial were less for the valaciclovir than the placebo recipients. The majority of these cost savings were attributable to fewer and shorter hospital admissions and less use of concomitant medications. In addition, over the duration of the modeled evaluation, valaciclovir-treated patients had fewer graft failures, less use of dialysis, and less need for re-transplantation. This translated into further cost savings for patients treated with valaciclovir prophylaxis.

Table 4. Cost of medical resources (first 6 months post-transplant)

	D+R−			R+		
Medical resource	Valaciclovir	Placebo	Difference	Valaciclovir	Placebo	Difference
Valaciclovir 500 mg capsules	$3904	$0	+$3904	$3589	$0	+$3589
Inpatient hospital admissions	$13 947	$16 181	−$2234	$12 363	$13 792	−$1429
Physician and home health visits	$604	$646	−$42	$572	$599	−$27
Special procedures (e.g. bronchoscopy, ultrasound)	$151	$149	+$2	$134	$124	+$10
Total laboratory procedures	$140	$144	−$4	$143	$149	−$7
Concomitant medications	$1702	$2080	−$378	$1722	$1953	−$231
Total	$20 448	$19 199	+$1249	$18 522	$16 616	+$1906

Table 5. Cost-effectiveness results of the modeled evaluation

	Cost	Life-years	Incremental cost per life-year gained[a]	QALYs	Incremental cost per QALY gained[b]
D+R− patients					
Valaciclovir	$91 454	11.49		7.98	
No prophylaxis	$95 073	11.16		7.71	
Incremental	−$3619	0.33	Dominant[c]	0.27	Dominant[c]
R+ patients					
Valaciclovir	$89 773	11.48		7.97	
No prophylaxis	$88 858	11.41		7.91	
Incremental	+$914	0.07	$13 931	0.05	$17 127

QALY, quality-adjusted life year.
[a]Incremental cost of valaciclovir divided by incremental number of life-years gained.
[b]Incremental cost of valaciclovir divided by incremental number of QALYs gained.
[c]Intervention provides greater benefits and lower costs.

Table 6. Sensitivity analysis

	Incremental cost per life-year		Incremental cost per QALY	
Variable tested	D+R−	R+	D+R−	R+
Base case	Dominant[a] (−$3619, 0.33)	$13 931	Dominant (−$3619, 0.27)	$17 127
Undiscounted	Dominant (−$4343, 0.70)	$5125	Dominant (−$4343, 0.54)	$6602
Relative risk of graft failure is halved for CMV−/AR+ and CMV+/AR+ patients	Dominant (−$1132, 0.15)	$49 031	Dominant (−$1132, 0.13)	$60 117
Trial based hospital cost savings in valaciclovir-treated patients are not realized	Dominant (−$1385, 0.33)	$35 702	Dominant (−$1385, 0.27)	$43 894
Trial based concomitant medication cost savings in valaciclovir-treated patients are not realized	Dominant (−$3242, 0.33)	$17 450	Dominant (−$3242, 0.27)	$21 454
Duration of model is 10 yr	Dominant (−$3737, 0.11)	$49 076	Dominant (−$3737, 0.10)	$48 838
Differences between treatment groups in proportion of patients with each CMV/AR outcome is increased by 50%	Dominant (−$5191, 0.44)	$9221	Dominant (−$5191, 0.35)	$11 345
Differences between treatment groups in proportion of patients with each CMV/AR outcome is decreased by 50%	Dominant (−$1174, 0.16)	$43 437	Dominant (−$1174, 0.13)	$53 397

[a]Dominant: valaciclovir has greater health outcomes and lower costs. The figures in brackets represent the cost savings and outcome gains associated with valaciclovir therapy. For example, 'Dominant (−$3619, 0.33)' means that valaciclovir prophylaxis was associated with $3619 lower costs per patient and 0.33 more life-years.

Outcomes

The modeled outcomes of treatment were measured in life-years and QALYs. Over the 30-year period of the model, valaciclovir-treated patients gained a greater number of life-years and QALYs than patients not receiving prophylaxis. D + R− patients treated with valaciclovir prophylaxis gained an extra 0.33 life-years and 0.27 QALYs. R + patients treated with valaciclovir prophylaxis gained extra 0.07 life-years and 0.05 QALYs. These benefits were because of lower rates of graft failure in valaciclovir-treated patients. Patients with a functioning graft have a better quality of life (17) and lower risk of mortality (19) than patients with a failed graft.

Cost-effectiveness

Table 5 shows that the total health care cost over the duration of the modeled evaluation was $3619 lower for D + R− patients treated with valaciclovir prophylaxis than those not receiving prophylaxis. Thus, given that these patients also had better survival and quality-adjusted survival, valaciclovir prophylaxis was a dominant strategy compared with placebo.

Each R + patient treated with valaciclovir prophylaxis incurred an incremental cost of $914. Incremental cost-effectiveness ratios represent the extra spending required to gain an additional unit of benefit and are calculated as the extra cost of therapy divided by the extra benefits of that therapy. The incremental cost per life-year and QALY ratios for R + patients were $13 931 and $17 127, respectively.

Sensitivity analysis

The sensitivity analysis results are given in Table 6. They indicate that the cost-effectiveness results are robust to changes in key variables. In each of these

cases valaciclovir prophylaxis was dominant in D+R− patients and was cost-effective in R+ patients.

For example, the sensitivity analysis considered the effects of CMV disease and AR on the risk of graft failure. The risk of graft failure for patients with AR relative to those without AR was halved at each cycle in the Markov process in order to show the extent of the effect of this model parameter on the results of the economic evaluation. Under this assumption, valaciclovir prophylaxis was a dominant intervention (greater benefits and lower costs) in the D+R− population and cost-effective in R+ patients.

Reducing the duration of the economic model from 30 to 10 yr reduced the relative cost-effectiveness of valaciclovir in R+ patients. The incremental cost per life-year gained of valaciclovir prophylaxis increased from $13 931 to $49 076. This result is not unsurprising given that 10 yr is an inadequate period over which to capture the entire loss of life-years associated with excess mortality in patients not receiving valcicolovir. Nevertheless, an incremental cost per life-year gained of $49 076 remains within the bounds of reasonable cost-effectiveness.

Discussion

The purpose of this study was to evaluate the cost-effectiveness of valaciclovir for the prophylaxis of CMV infection and disease in patients undergoing renal transplantation. The evaluation was conducted from the perspective of Australian health care providers and incorporated the longer term costs and final health outcomes associated with CMV disease and AR.

Final outcomes, such as QALYs and life-years, are important in economic evaluation as they provide a standard unit for measuring benefit, thus enabling comparisons of cost-effectiveness across a range of therapeutic areas. Governments and health care policy makers require information on final outcomes to allocate a finite health care budget across different therapeutic areas. Previous economic evaluations of valaciclovir prophylaxis have not considered final outcomes of therapy.

Legendre et al. performed a 'trial-based' economic evaluation which compared the cost and health outcomes of valaciclovir prophylaxis and no prophylaxis within the trial period (13). This meant that the outcomes considered by the evaluation were limited to those observed in the trial. The Lowance et al. trial was not of sufficient duration or statistical power to capture the effects of valaciclovir prophylaxis on final health outcomes such as graft failure, quality of life, and mortality (1).

Mauskopf et al. used a decision-tree model to estimate the cost-effectiveness of a range of therapies including valaciclovir prophylaxis as well as other prophylaxis, pre-emptive, and 'wait-and-treat strategies' (14). Their results, presented as cost per patient free of CMV disease, do not allow a comparison of the cost-effectiveness of CMV prophylaxis and treatment strategies relative to health care interventions in other therapeutic areas. The results of this evaluation, presented as cost per life-year gained and cost per QALY gained do allow such comparisons.

This evaluation showed valaciclovir prophylaxis has greater cost-effectiveness in D+R− patients than R+ patients. This result is not unexpected, as D+R− patients are at greatest risk of CMV disease and therefore have the greatest capacity to benefit from valaciclovir prophylaxis. However, valaciclovir prophylaxis in R+ patients still represented a cost-effective intervention. An incremental cost per QALY of $17 127 is well below that of many other health care interventions (20). For example, the incremental cost per QALY gained of hospital haemodialysis has been reported at over £20 000 ($56 000) (21).

Prior to the Humar et al. study (18), the long-term effects of CMV disease were not well understood. Therefore, economic evaluations with long time horizons could not be sensibly undertaken. This analysis found the long-term consequences of CMV are costly and lead to high morbidity and mortality. The poor clinical outcomes result from higher rates of graft failure and associated mortality. The costs of CMV are driven by an increased number of patients requiring dialysis and repeat transplantations. This analysis has found the use of valaciclovir in renal transplantation for the prophylaxis of CMV disease is a cost-effective intervention, which significantly reduces the burden of CMV infection and disease on patients and the health care system.

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