The Economic Value of Valacyclovir Prophylaxis in Transplantation

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Cytomegalovirus (CMV) infection and disease, with its extensive direct and indirect consequences, adds considerably to the cost of patient management in both solid organ and bone marrow transplantation. Antiviral prophylaxis for CMV infection can offer cost advantages over preemptive therapy and “wait-and-treat” approaches. Valacyclovir has demonstrated efficacy for CMV prophylaxis in renal, heart, and bone marrow transplantation and is cost-effective when compared with placebo in renal transplant recipients at high risk of CMV infection. In reducing CMV infection and disease, valacyclovir prophylaxis appears to be associated with reductions in indirect effects of CMV (acute graft rejection, other opportunistic infections) and, if these effects are considered, the potential exists for even greater savings to be made with valacyclovir therapy. Benefits of valacyclovir in transplantation extend beyond CMV to other herpesviruses and may be increased in some clinical situations by prolonging prophylaxis beyond 3 months.

The high cost of infectious complications in organ transplantation is measured not only in increased morbidity and mortality but also in economic terms. New potent immunosuppressive agents have decreased the incidence of graft rejection but leave the patient highly susceptible to fungal, bacterial, and viral infections. Cytomegalovirus (CMV), one of the most common opportunistic infections after organ transplantation, is associated with considerable mortality [1, 2]. In addition to direct CMV disease causing pneumonitis, enteritis, and hepatitis, indirect effects are increasingly recognized, such as enhanced immunosuppression, leading to further increased frequency of opportunistic infections and decreased graft and patient survival [3–5].

The high prevalence of CMV infection (50%–60%) in the general population [6] means that most transplant recipients are seropositive (R⁺) for CMV, and it is difficult to find CMV-seronegative donors (D⁻) for uninfected recipients. Combinations of CMV-seropositive donor (D⁺) and CMV-seronegative recipient (R⁻) are at greatest risk of development of CMV infection and disease after transplantation [7, 8]. The risk for CMV infection or reactivation is greatest in persons most heavily immunosuppressed, which may relate to the immunosuppressive regimen used and/or the duration of immunosuppression since surgery or engraftment.

The increased costs incurred when an organ transplant recipient develops CMV disease have been studied in a number of clinical settings. In a study of liver transplantation recipients, CMV disease was associated with a median increase in length of hospital stay of 30 days (64 vs. 34) and an increased cost of transplantation of about $58,000 [9]. In another study, CMV disease in liver transplant patients was associated with an increase in costs for the first 120 days from $114,100 to $148,300, adjusted to 1990 costs [10]. Asymptomatic CMV infection resulted in a nonsignificant increase in costs to $118,600.

In renal transplantation, a Canadian retrospective case-controlled study found that mean hospital costs were 2.5 times higher in patients with organ-specific CMV disease than in disease-free controls [11]. Patients developing CMV disease required on average 59 hospital stay days during the first year after transplant (range, 9–132) versus 22 days in the control group (range, 8–114; P = .001). A US study estimated increases in length of hospital stay for patients with CMV infection of 12–23 days and incremental hospital costs of $5600–$12,500 (1987 values) compared with uninfected patients [12].

Economics of CMV Prophylaxis versus Preemptive Therapy

There are many choices for the management of CMV infection and disease in transplant recipients. CMV prophylaxis involves continuous therapy with antiviral medication during the period when patients are most at risk of CMV infection or reactivation; most clinical protocols advise regular monitoring for evidence of CMV reactivation. Preemptive management requires more vigilant and frequent monitoring for CMV antigen or DNA, followed by high-dose CMV-specific antiviral therapy for those in whom the early signs of CMV infection are detected. Waiting until CMV disease manifests before administering antiviral therapy requires very aggressive, higher dose regimens, which can lead to increased patient morbidity and greater need for hospital care. This is the least desirable treatment modality [11, 12].
While drug costs for antiviral prophylactic therapy are not insignificant, the alternative approach, preemptive therapy to prevent CMV end organ invasive disease, does not eliminate CMV disease and CMV viremia may recur in up to 25% of patients [13]. Waiting until CMV infection is detected before treating CMV necessitates the use of more potent antiviral agents. The only agent currently licensed for this indication is intravenous ganciclovir, which is associated with a significant risk of neutropenia and increased need for patient hospitalization [14, 15]. Valganciclovir, an orally administered prodrug of ganciclovir, achieves serum levels similar to intravenous ganciclovir [16]. The safety and efficacy of valganciclovir is currently being assessed for the prevention of CMV disease in transplant patients.

CMV prophylaxis with valacyclovir decreases the risk of acute graft rejection in renal transplantation [17]. No similar effect has been shown for preemptive antiviral strategies. Prophylaxis with oral valacyclovir or intravenous ganciclovir has been compared with two strategies involving monitoring for viral shedding and a “wait-and-treat” management approach in an economic model applied to CMV-seronegative recipients of CMV-seropositive kidney transplants in the United Kingdom [18]. Five management options were considered in the decision analysis model: (1) prophylaxis with intravenous ganciclovir 700 mg/day on posttransplantation days 14–28; (2) prophylaxis with oral valacyclovir 8000 mg/day for 90 days starting within 72 h of transplantation; (3) monitoring for CMV reactivation by shell vial culture and preemptive therapy with intravenous ganciclovir beginning when viral shedding is detected; (4) monitoring for CMV reactivation by shell vial culture, adjustment of immunosuppression, and intensive monitoring for viral shedding and clinical symptoms when viral shedding is detected; and (5) wait-and-treat with CMV-specific therapy (with or without maintenance ganciclovir) once CMV syndrome or tissue-invasive disease occurs.

The impact of each strategy on the incidence of CMV disease and drug-related adverse events was estimated from published literature. Cost data for 1996 were extracted from the British National Formulary [19] and from a publication presenting unit costs for health care services used for prophylaxis against fungal infections in an immunocompromised population [20]. The expected cost and number of cases of CMV disease were calculated for each management strategy and then used to compute incremental cost-effectiveness ratios.

Prophylaxis for CMV with both valacyclovir and intravenous ganciclovir was less costly and at least as effective as preemptive therapy, adjusting the immunosuppression and wait-and-treat strategies [18]. Oral valacyclovir prophylaxis for 90 days was more effective but more costly than intravenous ganciclovir prophylaxis (14 days). When assuming the incidence of CMV disease in D+R+ renal transplant patients without preventative intervention is between 45% and 60% [17, 21], the cost difference between prophylaxis with intravenous ganciclovir and oral valacyclovir is $223–$621 per patient. As often occurs with modeling initiatives, there was an accepted degree of uncertainty around some input parameters, including the cost of treating CMV disease and the associated morbidity. If the indirect effects of CMV disease (increased risk of graft rejection and opportunistic infections) are taken into account and the total cost of CMV disease increases by 80% or more, oral valacyclovir prophylaxis becomes a cost-saving intervention compared with intravenous ganciclovir prophylaxis [18]. The greater the costs associated with managing CMV disease, the more cost-effective oral valacyclovir prophylaxis becomes.

An additional health outcome in the management of CMV disease is the quality of life of patients receiving intravenous ganciclovir, with its attendant adverse event profile including neutropenia and requirement for intravenous therapy. Not surprisingly, most patients prefer the option of oral over intravenous therapy [22, 23].

**Economics of Valacyclovir Prophylaxis in Transplantation**

CMV prophylaxis in renal transplantation. In a randomized trial examining the effect of CMV prophylaxis with valacyclovir, 616 renal transplant recipients were assigned to valacyclovir (2000 mg 4 times/day) or placebo for 90 days after transplantation, with the dose adjusted according to renal function [17]. Of the patients, 34% were CMV-seronegative recipients of a kidney from a seropositive donor and 66% were CMV-seropositive recipients. The incidence of CMV disease during the 6-month observation period after transplantation was significantly lower for patients given valacyclovir prophylaxis. In seronegative patients, the incidence of CMV disease was 45% for placebo recipients and 16% in valacyclovir recipients (hazard ratio [HR], 0.22; 95% confidence interval [CI], 0.12–0.40; P < .001). Among the seropositive patients, the respective values were 6% and 1% (HR, 0.18; 95% CI, 0.04–0.83; P = .03). In the higher risk CMV-seronegative group, valacyclovir also significantly reduced the rate of acute graft rejection and the risk of nonherpesvirus infections (see below).

Medical resource use and efficacy data collected from this study were used for an economic evaluation of valacyclovir for CMV prophylaxis in renal transplantation from the perspective of the French health care system [24]. Information was recorded as number of hospital admissions, days hospitalized, type of ward (intensity of nursing care), physician consultations, special procedures (e.g., magnetic resonance imaging, radiographs), laboratory tests, and days of medication (including ganciclovir) use during the 6-month posttransplant period. Data were also collected on outpatient resource use including numbers of physician consultations, home health care visits, special procedures, and laboratory tests. French unit costs for 1998 were applied in the economic analysis and here are converted into Euros (€) and US dollars (US$).
Significantly fewer inpatient resources were required by CMV-seronegative patients administered valacyclovir prophylaxis compared with placebo recipients [24]. Differences were evident in the number of hospital admissions, total hospital days, number of special procedures, and the number of laboratory tests. On average, the valacyclovir group needed 5.5 fewer days of inpatient hospitalization (26.9 vs. 32.4; \( P = .04 \)). Valacyclovir patients also required significantly fewer days of ganciclovir therapy (2.1 vs. 7.7; \( P < .001 \)) and oral acyclovir therapy (1.6 vs. 5.5; \( P = .005 \)).

In the seropositive group, there were significantly fewer hospital admissions among valacyclovir recipients than placebo recipients (1.8 vs. 2.1; \( P = .01 \)) and significantly fewer days of ganciclovir (0.5 vs. 1.5; \( P = .05 \)) and acyclovir (1.6 vs. 7.7; \( P = .001 \)). Other inpatient- and outpatient-resource use was similar across the two treatment groups.

For seronegative patients, the clinical benefits of valacyclovir prophylaxis were associated with overall mean savings of €1484 ($1298) per patient compared with placebo (table 1) [24]. The cost of valacyclovir was more than offset by cost savings in other resources such as special procedures, laboratory tests, and, in particular, hospitalization costs. A saving of €2832 ($2477) per patient resulted from fewer days in the hospital. In this high-risk group, valacyclovir was the economically superior strategy compared with placebo recipients ($2477) per patient resulted from fewer days in the hospital. In such patients, CMV is associated with a high rate of morbidity and with more deaths than any other infectious agent [25]. In a large double-blind controlled trial, 748 allogeneic BMT patients were randomized to oral valacyclovir 2000 mg 4 times daily or oral acyclovir 800 mg 4 times daily starting from engraftment or 4 weeks after BMT. All patients were given intravenous acyclovir (500 mg/m² 3 times/day) from the day of engraftment until engraftment. Valacyclovir and ganciclovir prophylaxis in a randomized open-label parallel study in CMV-seropositive allogeneic BMT recipients [26]. All received intravenous acyclovir (500 mg/kg 2 times/day for 1 week, followed by 6 mg/kg once daily for 5 days/week to 100 days after BMT). All patients were given intravenous acyclovir (500 mg/m² 3 times/day) from the day of transplantation until engraftment. Valacyclovir and ganciclovir recipients had similar rates of CMV infection, CMV disease, other opportunistic infections, survival, and acute or chronic graft-versus-host disease (GVHD).

Findings for valacyclovir versus ganciclovir were as follows: survival, HR, 1.310 (95% CI, 0.819–2.096; \( \text{P} = .259 \)); CMV disease, HR, 1.943 (95% CI, 0.176–21.44; \( \text{P} = .588 \)); CMV infection, HR, 0.593 (95% CI, 0.271–1.296; \( \text{P} = .190 \)); other opportunistic infections, HR, 1.008 (95% CI, 0.733–1.388; \( \text{P} = .959 \)); acute GVHD, HR, 0.935 (95% CI, 0.604–1.445; \( \text{P} = .761 \)), and chronic GVHD, HR, 1.235 (95% CI, 0.610–2.500; \( \text{P} = .557 \)). Valacyclovir was well tolerated and associated with less neutropenia or leukopenia than intravenous ganciclovir (18% vs. 38%). In BMT recipients, effective CMV prophylaxis with valacyclovir offers the convenience of an oral therapy and has the potential for economic advantages over both preemptive therapy and prophylaxis with intravenous ganciclovir.

<table>
<thead>
<tr>
<th>Resource</th>
<th>Difference between valacyclovir and placebo, € ($US)</th>
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<tbody>
<tr>
<td>Inpatient</td>
<td></td>
</tr>
<tr>
<td>Renal transplant unit care (days)</td>
<td>−2359 (2065) −483 (422)</td>
</tr>
<tr>
<td>Intensive care unit (days)</td>
<td>−318 (279) −106 (93)</td>
</tr>
<tr>
<td>Regular hospital (days)</td>
<td>−154 (135) −309 (270)</td>
</tr>
<tr>
<td>Outpatient</td>
<td></td>
</tr>
<tr>
<td>Physician consultations</td>
<td>−7 (6) −14 (12)</td>
</tr>
<tr>
<td>Home healthcare visits</td>
<td>−4 (3) −2 (1)</td>
</tr>
<tr>
<td>Special procedures</td>
<td>−5 (4) −4 (4)</td>
</tr>
<tr>
<td>Laboratory tests</td>
<td>−8 (7) −14 (12)</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
</tr>
<tr>
<td>Ganciclovir</td>
<td>−44 (38) −8 (7)</td>
</tr>
<tr>
<td>Valacyclovir</td>
<td>1415 (1238) 1415 (1238)</td>
</tr>
<tr>
<td>Total costs</td>
<td>−1484 (1299) 476 (416)</td>
</tr>
</tbody>
</table>

NOTE. Data are by permission of Legendre et al. [24]. Negative values represent net cost saving for valacyclovir treatment over placebo. Unit costs expressed in Euros (€) and US dollars ($US). D’R’, donor cytomegalovirus (CMV) seropositive, recipient CMV seronegative; R’, recipient CMV seropositive.
as prophylaxis against herpes simplex virus (HSV) reactivation. Valacyclovir delayed the median time to CMV antigenemia from 19 days in the acyclovir group to 119 days (HR, 0.42; 95% CI, 0.18–0.99; \( P = .049 \)). CMV infection, symptomatic CMV infection, and CMV disease were similarly delayed by about 100 days. There were also trends for delayed acute rejection and for fewer opportunistic infections in the valacyclovir group.

No economic analyses have been done for use of valacyclovir in BMT or heart transplantation, but the benefits of an effective well-tolerated oral medication in these clinical settings are likely to extend to medical resource use. An effective oral therapy would avoid the hospitalization costs associated with intravenous drug administration and the risk of infection at the injection site. In addition, valacyclovir prophylaxis reduces the need for ganciclovir preemptive therapy. Valacyclovir as a “ganciclovir-sparing regimen” reserves ganciclovir for treating established CMV disease and has the advantages of better safety and less opportunity for drug resistance to develop.

Indirect effects of CMV infection in solid organ transplantation. In the large renal transplant study of Lowance et al. [17], valacyclovir prophylaxis of CMV infection and disease was associated with a significantly reduced rate of biopsy-confirmed acute graft rejection in D’R+ patients from 52% in the placebo group to 26% (HR, 0.43; 95% CI, 0.27–0.70; \( P = .001 \)). Clinical acute rejection was also reduced in this group from 61% to 39% (HR, 0.55; 95% CI, 0.37–0.83; \( P = .004 \)). Similarly, in the heart transplant study of Egan et al. [28], the first graft rejection episode was delayed by valacyclovir compared with low-dose acyclovir (HR, 0.51; 95% CI, 0.22–1.19; \( P = .091 \)), although statistical significance was not achieved with the small numbers of patients of this study.

Exploratory analysis with logistic regression analysis was conducted to determine whether the observed decrease in acute graft rejection with valacyclovir in renal transplantation [17] was associated with decreased CMV infection and disease [29]. Overall, CMV-seronegative transplant recipients who developed CMV disease were 1.87 times more likely to be biopsy-confirmed acute graft rejection than those without CMV disease (odds ratio [OR], 1.87; 95% CI, 0.97–3.63; \( P = .063 \); table 2), an association that approached statistical significance. There was a significantly higher rate of graft rejection in patients with confirmed CMV disease in the R+ arm, although the number of subjects was very small (n = 11, placebo group; n = 2, valacyclovir group; OR, 3.49; 95% CI, 1.11–10.98; \( P = .033 \)). An association between CMV viremia and acute graft rejection was less clear from the available data (D’R+ group, OR, 1.21; 95% CI, 0.63–2.30; \( P = .568 \); R+ group, OR, 1.59; 95% CI, 0.97–2.60; \( P = .065 \)).

ORs may suggest that CMV viremia is not sufficient to increase the risk of graft rejection and that the association requires the higher levels of CMV replication that stimulate clinical manifestations. Alternatively, the prompt use of preemptive therapy permitted in this protocol may have masked an effect of early CMV reactivation on the risk of acute graft rejection. Of interest, even among patients without CMV disease or evidence of viremia, valacyclovir reduced the incidence of graft rejection compared with placebo in both the R+ and R− groups (i.e., 43% vs. 23% in D’R− patients without CMV disease). This suggests that not only CMV but also other herpesviruses against which valacyclovir is active (e.g., human herpesvirus type 6 or 7) may be associated with graft rejection.

Valacyclovir prophylaxis for CMV was associated with a decreased incidence of other herpesvirus and nonviral opportunistic infections in renal transplant recipients [17]. In addition to the protective effect of valacyclovir for HSV and varicella zoster virus (VZV), it significantly reduced the risk of all nonherpesvirus infections in CMV-seronegative recipients by almost half (HR, 0.51; 95% CI, 0.35–0.74; \( P = .001 \)). In particular, valacyclovir recipients had a lower rate of Candida (Kaplan-Meier estimates, 10% vs. 22%; \( P = .04 \)) and Staphylococcus infections (12% vs. 21%; \( P = .07 \)) than placebo recipients.

Valacyclovir also reduced opportunistic infections in CMV-seropositive heart transplant recipients by 64% compared with low-dose oral acyclovir [28]. Although exploratory analysis of the data in renal transplantation did not detect an association between CMV disease and opportunistic infections overall, it showed that Candida infections were nearly 3 times more likely to occur in D’R− patients with CMV disease than in those without CMV (OR, 2.91; 95% CI, 1.24–6.84; \( P = .014 \); table 3). In CMV-seropositive recipients, CMV disease was associated with an 8-fold increase in susceptibility to Candida infections (OR, 8.23; 95% CI, 2.61–25.99; \( P < .001 \)). The wide CI reflects the small numbers of patients with the end points of Candida and CMV disease. In contrast, the decreased incidence of Staphylococcus infection in valacyclovir recipients may be independent of CMV infection as no association was observed between CMV disease and Staphylococcus infection in either CMV-seronegative or -seropositive patients (table 3).

Potential Benefits of Prolonging Prophylaxis Beyond 90–100 Days

The clinical benefit of valacyclovir as CMV prophylaxis was shown in prospective studies that evaluated treatment for 90 or 100 days [17, 26–28]. However, the period of greatest risk of CMV reactivation after transplantation varies by such factors as type of transplant, immunosuppression regimen, CMV serostatus, and development of complications. Thus, in some settings, there may be a benefit in prolonging CMV prophylaxis beyond 90–100 days, provided the treatment continues to be well tolerated. In renal and heart transplantation, reactivation of CMV in patients allocated valacyclovir mainly occurred after the 90-day prophylaxis period [17, 28]. In BMT recipients, valacyclovir prophylaxis up to posttransplant week 18 demon-
strated continued benefit in preventing or delaying CMV viremia compared with high-dose oral acyclovir [26]. With the exceptions of a slight increase in the frequency of confusion and hallucination in renal transplant recipients receiving valacyclovir [17], the tolerability of high-dose valacyclovir in heart, renal, and BMT recipients did not differ from that of placebo or oral acyclovir [17, 26, 28].

The economic analysis of the renal transplant study showed that patients who developed CMV disease spent a mean of 45.2 days in hospital compared with 24.2 days for patients who remained free of CMV disease [24]. This analysis was done with medical resource data collected over a 6-month posttransplant period, 3 months beyond cessation of valacyclovir prophylaxis. Of the 16 D’R+ valacyclovir recipients with CMV disease, 13 developed disease after the 90-day treatment period had elapsed [17]. It is likely that had prophylaxis been extended, disease may have been prevented in many of these patients and hospital costs reduced further. The additional cost of valacyclovir may have been offset by savings in hospitalization and treatment with ganciclovir.

An observational study to examine the effect of prolonging valacyclovir prophylaxis in renal transplantation beyond 3 months found that extending prophylaxis up to 6 months was beneficial in terms of preventing CMV disease [30]. Of interest, in these patients, pp65 antigenemia was not predictive of CMV disease. This reinforces the potential for clinical and economic benefit from continuing therapy for more than 3 months in settings where the risk of CMV reactivation continues.

**Table 2. Incidence of biopsy-confirmed acute graft rejection in renal transplant recipients with cytomegalovirus (CMV) disease or viremia.**

<table>
<thead>
<tr>
<th>CMV disease</th>
<th>Confirmed (%)</th>
<th>Absent (%)</th>
<th>P for difference</th>
<th>CMV viremia</th>
<th>Confirmed (%)</th>
<th>Not detected (%)</th>
<th>P for difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>D’R+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valacyclovir</td>
<td>5/14 (36)</td>
<td>20/88 (23)</td>
<td></td>
<td></td>
<td>3/19 (16)</td>
<td>22/83 (27)</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>24/41 (59)</td>
<td>28/65 (43)</td>
<td></td>
<td></td>
<td>23/40 (58)</td>
<td>29/66 (44)</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>29/55 (53)</td>
<td>48/153 (31)</td>
<td>0.063</td>
<td></td>
<td>26/59 (44)</td>
<td>51/149 (34)</td>
<td>0.568</td>
</tr>
<tr>
<td>R+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valacyclovir</td>
<td>2/2 (100)</td>
<td>55/202 (27)</td>
<td></td>
<td></td>
<td>7/28 (25)</td>
<td>50/176 (26)</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>6/11 (55)</td>
<td>63/193 (33)</td>
<td></td>
<td></td>
<td>31/68 (46)</td>
<td>38/136 (28)</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>8/13 (62)</td>
<td>118/395 (30)</td>
<td>0.035</td>
<td></td>
<td>38/96 (40)</td>
<td>88/312 (28)</td>
<td>0.065</td>
</tr>
</tbody>
</table>

**NOTE.** Incidences are actual numbers of patients with biopsy-confirmed graft rejection at end of 6 months follow-up [29]. D’R+, donor CMV seropositive, recipient CMV-seronegative; R+, recipient CMV seropositive.

Other Herpesviruses in Transplantation

As a broad-spectrum antiviral agent, valacyclovir given prophylactically protects transplant recipients against infections caused by HSV and VZV in addition to CMV [31]. In renal transplantation, valacyclovir significantly reduced the risk of HSV disease in both D’R+ (HR, 0.33; 95% CI, 0.15–0.74; P < .01) and R+ patients (HR, 0.16; 95% CI, 0.09–0.30; P < .001) [15]. VZV disease was not observed in any of the valacyclovir recipients but developed in 2 (2%) of CMV-seronegative and 9 (4%) of seropositive placebo recipients. A higher incidence of HSV and VZV infections was also observed in heart transplant patients taking low-dose acyclovir compared with high-dose valacyclovir [28]. Only 4 valacyclovir recipients (29%) experienced an episode of HSV infection compared with 7 of those taking acyclovir (54%). Two patients in the acyclovir group (15%) had herpes zoster while the valacyclovir patients remained free of VZV disease.

The efficacy and cost of substituting valacyclovir for intravenous acyclovir for HSV prophylaxis in BMT was examined in an observational study [32]. Intravenous acyclovir in doses of 500–1500 mg/m²/day (about 5–15 mg/kg/day) is routinely used as prophylaxis for reactivation of HSV in the immediate posttransplant period. This study compared medical records of 125 patients who received oral valacyclovir (500 mg once daily) with records of those who received intravenous acyclovir (750 mg/m²/day) from the day before transplant to initial discharge from the hospital. The incidence of HSV infections was similar between the two regimens (data not provided). Due to inability to take oral medication, some valacyclovir recipients required a temporary switch to intravenous acyclovir for a few days. The drug acquisition cost of valacyclovir was $19,297 compared with $42,877 for intravenous acyclovir, a saving of $23,580 or 55%. Inclusion of other factors, such as preparation costs for drug administration, pharmacy time, and nursing supervision time, may result in an even greater saving.

**Conclusions**

As a consequence of the considerable impact of CMV infection on the success of transplantation, substantial resources are devoted to the care of patients with this complication. The complex mechanisms leading to indirect effects of CMV infection continue to be researched with emphasis on the risks of opportunistic infections and graft rejection. These serious sequelae mean that the goal of the clinician must be to prevent CMV reactivation and disease rather than just to treat it.

Economic modeling suggests that CMV prophylaxis is more cost-effective than preemptive therapy and treating overt disease in some clinical situations. Valacyclovir prophylaxis for CMV infection is cost-effective in high risk (D’R+) renal trans-
plant recipients, with fewer hospital days required, and a reduced requirement for other health care resources. The efficacy of valacyclovir in preventing graft rejection, especially if it results in an increased period of graft survival and reduces the need for retransplantation, provides the potential for further long-term resource savings. Long-term (5 years) follow-up of patients participating in the study described by Lowance et al. [17] is ongoing. The benefits of a well-tolerated oral prophylactic drug to prevent CMV infection in transplant patients are also likely to be great in terms of patient quality of life. The resource savings to be made with effective prevention of CMV infection may not have been fully realized to date.

References

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