Preemptive therapy for prevention of cytomegalovirus disease in kidney transplant recipients

Background and Objectives

Cytomegalovirus (CMV) infection is a major cause of morbidity in patients receiving solid organ transplants. Preemptive therapy is a suitable option to prevent CMV disease in kidney transplant (KT) recipients. A single center retrospective study has been performed to evaluate the impact of preemptive strategy on the incidence and outcome of CMV infection after KT.

Methods

All consecutive 421 patients (284 M, 137 F, mean age 54.1 years [range 20.3-75.9], 26 with HIV infection) who underwent KT (399 from deceased donor and 18 from living related donor) and kidney-pancreas transplant (4 HIV positive recipients) between January 2006 to December 2013 were included in the study. CMV-IgG testing was recommended as part of routine screening of all donors and recipients. All recipients were followed prospectively for CMV-DNAemia in whole blood by RT-PCR (Abbott Molecular Inc., IL, USA), weekly during the first 3 months after Tx, later monthly for the first year post-tx and whenever clinically indicated. CMV preemptive therapy (ganciclovir 5 mg/kg bid iv or valganciclovir 900 mg bid os) starting criteria are shown in Table 1. Antiviral therapy was continued until two consecutive negative CMV-DNA detection in peripheral blood. Recurrent episodes of active infection were treated with additional courses of therapy starting with CMV-DNA values >100,000 copies/mL

<table>
<thead>
<tr>
<th>CMV R seronegative</th>
<th>DNAemia ≥ 100,000 copies/mL</th>
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<tbody>
<tr>
<td>CMV R seropositive</td>
<td>DNAemia ≥ 100,000 copies/mL</td>
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<tr>
<td>Steroid boluses or ATG/OKT3 therapy for Rejection</td>
<td>Any value of DNAemia</td>
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Table 1 - Preemptive Antiviral Therapy Starting Criteria

Results

Patient survival at 1, 3 and 5 years was 96.7%, 93.6% and 89.4% and graft survival 95.4%, 90.3% and 84.9%, respectively. Eight patients had a primary graft non function. Pretransplant CMV screening results were available in all transplant recipients: 384 (91.2%) seropositive and 37 (8.8%) seronegative.

A total of 411/421 (97.6%) recipients (378 R+ and 33 R-) with a minimum follow-up of at least 30 days were clinically and virologically monitored for a mean of 77.6 months post-KT.

Primary CMV infection was observed in 22/25 (88.0%) D+/R- recipients at a median of 30 days (range 17-58) post-KT; 21 (95.5%) patients reached the threshold of CMV-DNAemia and were treated, for a median of 40 days (range 18-111); two recipients had mild clinical symptoms (Figure 1). Two pre-KT seronegative recipients developed asymptomatic CMV viremia after 6 months post-KT with spontaneous clearance.

CMV reactivation was observed in 191/378 (50.5%) of pre-KT seropositive recipients at a mean of 44.4 days (range 7-587) post-KT; 55 (14.6%) patients were treated for a mean of 22 days (range 5-78) (Figure 1). All patients were asymptomatic.

Among pre-KT seropositive recipients, a significantly greater proportion of patients receiving immunosuppressive therapy with everolimus were free from CMV reactivation when compared to the recipients on calcineurin inhibitor-based therapy without everolimus (65.5% vs 44.6%, P value <0.001) (Figure 2).

The incidence of CMV reactivation was significantly lower for the recipients who received basiliximab induction therapy compared to the recipients who received double induction with basiliximab plus antithymocyte globulins (40.3% vs 65.5%, p<0.001) (Figure 2).

Graft survival was similar for recipients who were treated with and without post-transplant CMV infection.

![Figure 1 - CMV Infections in KT Patients, Varese (Italy), 2006-2013](image1.png)

![Figure 2 - Incidence of CMV reactivation in R+ by immunosuppressive therapy](image2.png)

Conclusions

Our study confirms the safety and efficacy of preemptive therapy as preventive strategy for CMV disease in kidney transplant recipients.