

Editor's Note

Preventing Cytomegalovirus Infection After Liver Transplant An Evolving Approach

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Despite recent advances in the management of patients following liver transplant, cytomegalovirus (CMV) infection remains a substantial cause of morbidity and mortality among this population.¹ Clinicians and transplant centers have adopted



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varying approaches to managing CMV-seronegative liver transplant recipients with CMV-seropositive donors, a recipient group that is at highest risk for developing CMV-associated complications. Antiviral prophylaxis is typically initiated soon after transplant for a period of several months. Although the most widely used strategy, prophylaxis is limited by the incidence of delayed-onset CMV disease that can occur long after antivirals are completed. In contrast, preemptive therapy involves monitoring patients for CMV viremia and beginning antivirals only after CMV replication is detected by polymerase chain reaction testing. Small, observational studies have suggested that preemptive therapy in this high-risk population may be associated with lower rates of CMV disease.

In this issue of *JAMA*, Singh et al² report the findings of a multicenter, randomized clinical trial that compared preemptive therapy vs antiviral prophylaxis on the incidence of CMV disease in seronegative liver transplant recipients with seropositive donors. In this trial, 205 patients were randomly as-

signed to receive either preemptive therapy or antiviral prophylaxis using valganciclovir, and were followed up for at least 12 months. The primary outcome, incidence of CMV disease by 12 months after transplant, was significantly lower among those who received preemptive therapy vs antiviral prophylaxis (9% vs 19%). This finding was primarily due to a reduction in delayed-onset disease (6% for preemptive therapy vs 17% for antiviral prophylaxis). In an exploratory analysis, the authors also report the measurement of CMV-specific immune responses to both preventive strategies, a unique aspect of this study.

While these results provide some clarity regarding the use of preemptive therapy, several caveats remain. Preemptive therapy requires weekly monitoring by serum polymerase chain reaction and immediate initiation of antivirals when indicated. Transplant centers may differ in their capacity to support such frequent measures, and some patients may find these requirements costly, and logistically burdensome, especially if this specialized test is not easily available locally. The authors appropriately note that the decision to pursue preemptive therapy will ultimately depend on institutional capacity and available resources. Despite these limitations, preemptive therapy may be a viable option for preventing CMV infection among selected high-risk patients following liver transplant.

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2. Singh N, Winston DJ, Razonable RR, et al. Effect of preemptive therapy vs antiviral prophylaxis on cytomegalovirus disease in seronegative liver transplant recipients with seropositive donors: a randomized clinical trial. Published April 14, 2020. *JAMA*. doi:10.1001/jama.2020.3138