Late Reactivation of Cytomegalovirus With Letermovir Use in Allogeneic Stem Cell Transplant

Cytomegalovirus (CMV) reactivation occurs in 60%-70% of CMV-seropositive patients undergoing allogeneic stem cell transplantation (ASCT) and is associated with high mortality rates. Letermovir is a prophylactic antiviral agent indicated for the prevention of CMV reactivation up to 100 days post-ASCT, however, evidence for its use beyond 100 days is lacking.

This study evaluated the rate of clinically significant late CMV reactivation, defined as requiring preemptive treatment, in patients receiving letermovir or alternative CMV preventative therapy for at least two weeks prior to day +100. Secondary objectives included the time to clinically significant CMV infection, factors contributing to late CMV reactivation, and the incidence of resistant CMV infections.

In this retrospective, matched cohort, single-center study, CMV-seropositive patients treated with letermovir plus acyclovir were identified between May 1st, 2018 and March 31st, 2020. Letermovir patients were matched in a 1:1 ratio with CMV-seropositive patients who received alternative CMV preventative therapy alone (e.g. acyclovir, valacyclovir, and/or ganciclovir). Patients were followed through at least day +180 post-transplant.

The incidence of late CMV reactivation with letermovir use, compared to alternative therapy, was 53% versus 36% ($P=0.0275$). The average time to clinically significant CMV infection was 167 days in the letermovir group and 81 days for alternative therapy ($p<0.001$). Corticosteroid use at the time of reactivation was the only identified risk factor associated with an increased rate of late CMV reactivation in the letermovir group. There was no difference in the rate of resistant CMV infections between the groups.

Letermovir use for CMV prevention, compared to alternative therapies, resulted in a significantly higher rate of late CMV reactivation in patients post-allogeneic stem cell transplantation. Time to CMV reactivation was notably longer in the letermovir group, indicating that letermovir use beyond day +100 post-transplantation may be warranted to reduce rates of late CMV reactivation.