1748. Incidence of Cytomegalovirus Disease and Viral Replication Kinetics in Intermediate Risk Liver Transplant Recipients Managed According to a Preemtive Therapy Algortihm

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Background. Cytomegalovirus (CMV) is an important opportunistic pathogen in liver transplant recipients (LTR). Risk of invasive disease is determined by CMV donor/recipient (D/R) serostatus, immunosuppression, and use of antiviral prophylaxis. Viral replication kinetics that can predict the development of CMV disease in transplant recipients are a high maximal viral load (VL) and a fast replication velocity. At our institution LTR at intermediate risk for CMV disease (CMV D/R+) are managed following a preemptive therapy algorithm (the pre-established cutoff for treatment initiation is 4,000 IU/mL). The primary endpoint of this study was to determine the incidence of early CMV disease in CMV D/R+ LTR. Secondary endpoints were to calculate the period of maximal VL and viral kinetic parameters.

Methods. We performed a retrospective observational study of CMV D/R+ LTR. Patients were followed for 6 months after transplantation. We calculated the incidence of CMV disease. Viral kinetic parameters calculated were the VL duplication time (Td) and the basic reproductive number (R0). For the assessment of viral kinetics we used the maximal VL of 10 patients who had a VL determined within the previous week.

Results. Forty CMV D/R+ LTR were included. The median age was 52 years, 65% were women. The mean MELD score was 18, 83% of patients had decompensated cirrhosis. No patient developed CMV disease during the first 6 months after LT. Nineteen patients (47%) had CMV DNAemia, but only 8 (20%) required antiviral therapy. The highest VLs were observed during the second month after transplant. The median duplication time was 2.14 days. The median R0 was 1.46.

Conclusion. Although limited by our sample size, our algorithm appears useful for discriminating the patients who need antiviral treatment from those who will only have asymptomatic DNAemia. The study population VL, Td and R0 behave as described by other groups, which emphasizes the need for frequent monitoring. This is a challenge for CMV prevention in resource-limited countries.

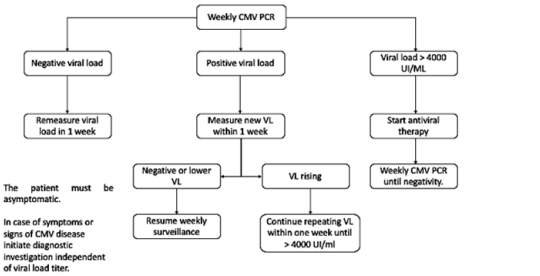

Figure 1. Preemptive therapy algorithm for liver transplant recipients at intermiediate risk for cytomegalovirus disease.

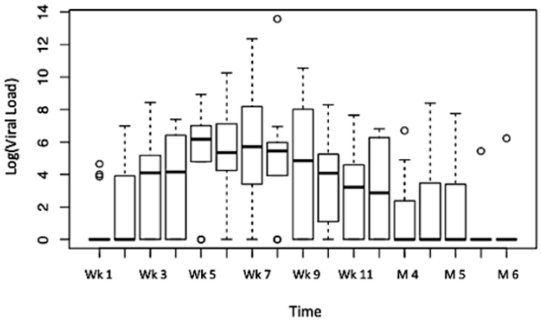

Figure 2. Distribution of cytomegalovirus viral load measurements over time.

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1749. A Nationwide Survey of Cytomegalovirus Prevention Strategies in Kidney Transplant Recipients in a Resource-Limited Setting

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Background. Cytomegalovirus (CMV) causes morbidity in kidney transplant (KT) recipients. Strategies to prevent this infection in resource-limited settings have been unreliably implemented and under-explored. We investigated CMV prevention strategies utilized among transplant centers in Thailand.

Methods. A questionnaire on CMV prevention strategies for KT recipients was developed using a web-based electronic survey website (www.surveymonkey.com). The survey was delivered to 31 transplant centers in Thailand. One infectious disease physician (ID) and one nephrologist (NP) from each center were included.

Results. There were 43 respondents from 26 (84%) transplant centers including 26 (60%) IDs and 17 (40%) NPs. The majority worked in a public hospital setting (63%) and had encountered KT recipients for at least 2 years (74%). Forty-one (98%) physicians agreed on the necessity of CMV prevention. Of these, 34 (81%) physicians implemented prevention strategies for their patients. Interventions included preemptive approaches (47%), prophylaxis (44%), hybrid approaches (3%); surveillance after prophylaxis (3%), and CMV-specific immunity-guided approaches (3%). For CMV-seropositive KT recipients, use of preemption (84%) exceeded prophylaxis (12%). However, 81% of the former preferred targeted prophylaxis in patients receiving anti-thymocyte globulin therapy. Sixty-five and 93% of physicians started preemptive therapy when plasma CMV DNA loads reached 2,000 and 3,000 copies/mL (1,820 and 2,730 IU/mL), respectively. A significantly greater percentage of NPs initiated preemptive therapy at a plasma CMV level of 1,820 IU/mL compared with IDs (88% vs. 50%, [$P = 0.02$]). The most common barrier to prevention strategy implementation was financial inaccessibility of oral valganciclovir (67%) and quantitative CMV DNA testing (12%). The majority (81%) felt that a guideline would allow physicians to implement CMV prevention strategies for their patients.

Conclusion. Most physicians agreed on a need for preemptive approaches, although prophylaxis was targeted in those receiving intense immunosuppression. Guidelines and financial accessibility could improve CMV prevention strategy implementation in Thai KT recipients.

Disclosures. **All authors:** No reported disclosures.

1750. Epidemiology of Cytomegalovirus DNAemia in Pediatric Solid-Organ Transplant Patients

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Background. Despite the widespread use of prevention strategies, CMV remains a common opportunistic infection in SOTR. Contemporary data regarding CMV in pediatric SOTR is limited. We sought to determine the frequency of and risk factors for CMV infection and disease in a large single-center cohort of pediatric SOTR.

Methods. A retrospective cohort study of patients <22 yr of age who received lung, heart, liver, kidney, or multi-organ transplants at TCH between 2014 and 2018 was completed. Universal CMV prophylaxis was used based on risk status (Figure 1). Primary outcome was CMV DNAemia (plasma level ≥ 1,000 IU/mL). Associations with CMV DNAemia were measured using Fisher exact, Kruskal–Wallis, and multivariate logistic regression. Survival analysis and time to CMV infection were assessed using Kaplan–Meier plots.

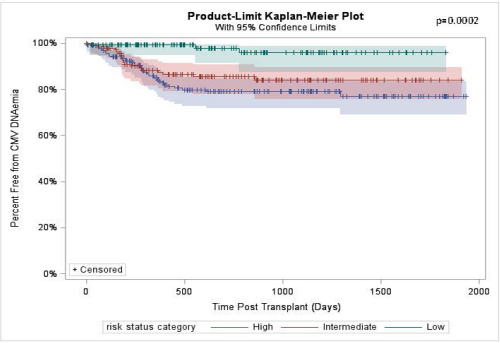
Results. Among 465 SOTR, 57 (12%) had CMV DNAemia ≥ 1,000 IU/mL; this included 9/52 (17%) lung, 22/155 (14%) liver, 16/125 (13%) heart, 1/9 (11%) multi-organ, and 9/124 (7%) kidney recipients. 6 (10%) SOTR had early-onset CMV reactivation while on antiviral prophylaxis. Post-prophylaxis, 48 (85%) SOTR had CMV reactivation and 3 (5%) had primary infection. Median time to DNAemia > 1,000 IU/mL was 366 days post-transplant for lung, 115 for liver, 185 for heart, and 290 for kidney ($P = 0.04$), reflecting differences in prophylaxis strategies. High-risk CMV status (D+/R- for heart, liver, kidney and D+ and/or R+ for lung) was associated with CMV DNAemia ($P < 0.01$, Figure 2). DNAemia was not associated with age at transplantation, type of organ, or induction immunosuppression. There was no difference in survival during the study follow-up period (1 – 5 years) for SOTR with vs. without DNAemia. Overall, 18/465 (4%) SOTR had CMV disease: 2 (4%) lung, 3 (2%) liver, 5 (4%) heart, 1 (11%) multi-organ, and 7 (6%) kidney recipients. 16 had CMV syndrome and 2 had tissue-invasive disease. Median (range) maximum viral loads were 35,768 IU/mL (3,239–4,807,992) for SOTR with vs. 2,605 IU/mL (1,000–112,000) for SOTR without CMV disease ($P < 0.01$)

Conclusion. This large contemporary cohort of pediatric SOTR on universal prophylaxis demonstrates low overall rates of CMV DNAemia and CMV disease. High-risk CMV status remains associated with CMV DNAemia, suggesting that further interventions targeting this group may be warranted.

Figure 1: CMV prevention regimens utilized 2014-2018 at TCH

Organ	Serostatus	Risk Status	Prophylaxis
Lung	D+/R- R+ D-/R-	High High Low	12 mo of ganciclovir/valganciclovir + CMV Ig 12 mo of ganciclovir/valganciclovir 3 mo of ganciclovir/valganciclovir
Heart	D+/R- R+ D-/R-	High Intermediate Low	3 mo of ganciclovir/valganciclovir + CMV Ig 3 mo of ganciclovir/valganciclovir + CMV Ig None
Liver	D+/R- R+ D-/R-	High Intermediate Low	6 mo of ganciclovir/valganciclovir 6 mo of ganciclovir/valganciclovir 3 mo of ganciclovir/valganciclovir
Kidney	D+/R- R+ D-/R-	High Intermediate Low	6 mo of ganciclovir/valganciclovir + CMV Ig 6 mo of ganciclovir/valganciclovir 6 mo of ganciclovir/valganciclovir

Figure 2: Kaplan-Meier plot of the percent of patients free from CMV DNAemia > 1000 IU/ml by CMV risk status



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1751. The Impact of Prophylactic Systemic Antibiotics (PSA) on *Cytomegalovirus* (CMV) Infection: A Post-hoc Analysis of a Randomized Controlled Trial (RCT) in Hematopoietic Cell Transplantation (HCT) Recipients

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Background. Prophylactic systemic antibiotics (PSA) during conditioning regimen-induced neutropenia after hematopoietic cell transplantation (HCT) reduce bacteremia but may disrupt the gut microbiota, potentially affecting viral immunity and risk for viral infections. Prior studies suggest a critical role of gut microbiota in the reconstitution of CMV-specific CD8+ T cells and in protection from respiratory viral infections after HCT (J Immunol 2007; 178: 5209; Blood 2018; 131:2978). To identify whether PSA is associated with differences in CMV infection outcomes after HCT, we conducted a post-hoc analysis of CMV infection in the only RCT of PSA exclusively performed in HCT recipients (Infection 1986; 14:115). In that trial, HCT patients received either PSA (ticarcillin/tobramycin/vancomycin or mezlocillin/ceftizoxime) or no systemic antibiotics during neutropenia (absolute neutrophil count <500/mm^3).

Methods. A post-hoc analysis was performed of a previously conducted RCT in the pre-antiviral era (1984–1986) at the Fred Hutch. Patients received unscreened blood products and were tested weekly by CMV culture in throat, and disease was evaluated by tissue biopsy or bronchoalveolar lavage. CMV disease was confirmed by chart review. We compared the cumulative incidence of CMV at any site, CMV throat shedding, and CMV disease between randomization groups by day 100 post-transplant, treating death as a competing risk. Overall survival was also compared using Kaplan–Meier method.

Results. 119 and 125 allograft recipients were randomized to PSA and no prophylaxis, respectively. Baseline characteristics in both groups were balanced. CMV infection at any site and CMV throat shedding were greater in the PSA group (Figures 1 and 2); CMV disease was numerically reduced in the no PSA group (Figure 3). Overall survival by day 100 was not different between the groups (Figure 4).

Conclusion. CMV infection risk appeared to be increased in recipients of PSA with a significant anaerobic spectrum. While current PSA regimens have narrower spectrum activity, these results provide the rationale to study if changes in gut microbiota play a role in CMV reactivation and adaptive immunity after HCT.

Figure 1. Cumulative Incidence Plot of Time to 1st Any CMV

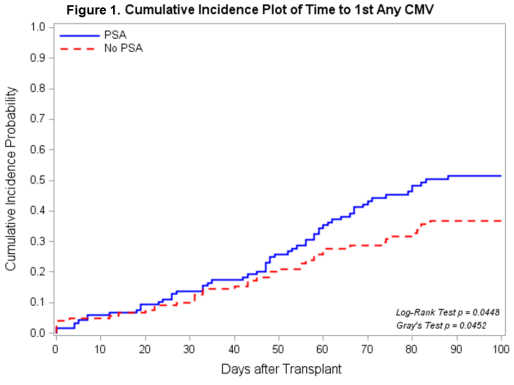


Figure 2.Cumulative Incidence Plot of Time to 1st CMV in Mouth, Throat, Upper Respiratory

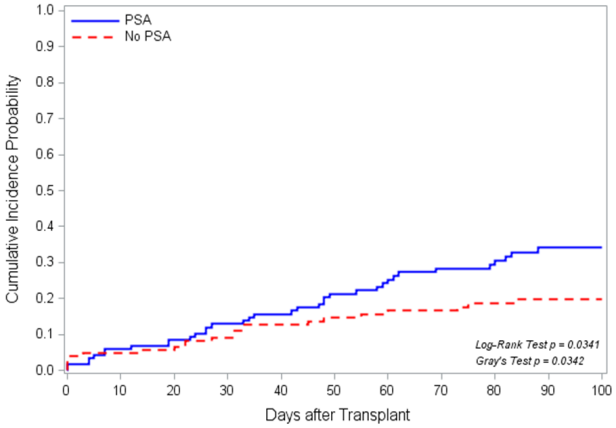


Figure 3. Cumulative Incidence Plot of Time to 1st Any Endorgan Disease

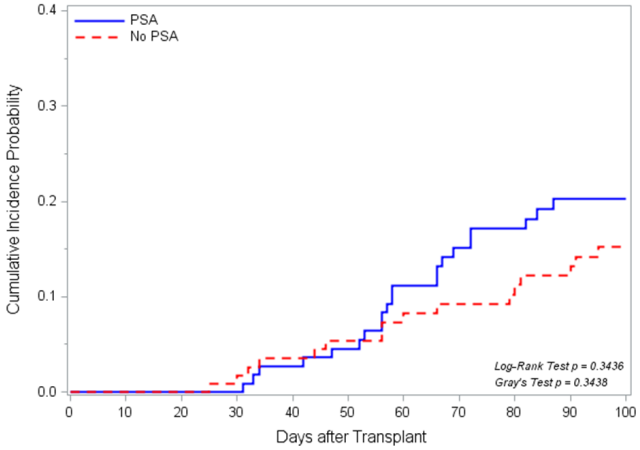
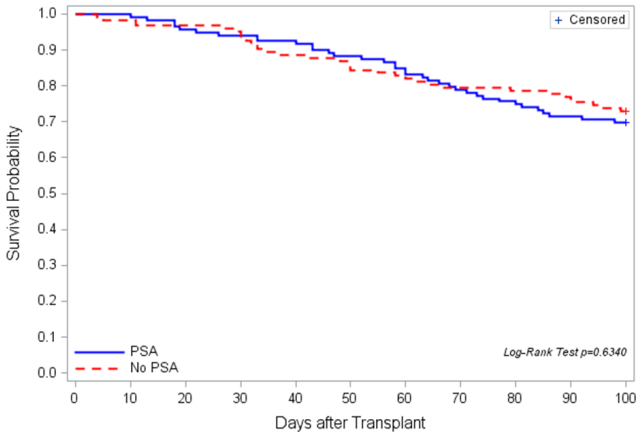


Figure 4. Kaplan Meier Plot of Time to Overall Mortality
Total Number of Events = 69



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1752. Differential Degree and Duration of Cytomegalovirus (CMV) Viremia Between WHO International Standard-Calibrated Quantitative CMV Nucleic Acid Tests: Implications for Clinical Care

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Background. Quantitative nucleic acid amplification (QNAT) tests are cornerstone for the management of CMV disease after organ transplantation. We assessed the potential impact of viral load results obtained by two commercial WHO international