# #2341. KINETIC FEATURES OF DOUBLE STRANDED DNA VIRUS DETECTION AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

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## Study Design and Conclusions

### Background

- Double-stranded DNA (dsDNA) virus detection is frequent after allogeneic hematopoietic cell transplantation (HCT).
- Improved understanding of virus kinetics and associated risk factors is important for the study of novel therapeutic strategies.

### Materials

- Weekly plasma samples through 100 days post-HCT were retrospectively tested by quantitative PCR for HHV-6A and B, BK virus (BKV), adenovirus (AdV), and EBV; tests for CMV were obtained from clinical records.

### Methods

- Adult and pediatric HCT recipients with ≥1 year of follow up and availability of ≥60% of samples while alive were included.
- The cohort consisted of 125 cord blood, 116 mismatched, and 156 matched HCT recipients (total N = 404).
- Average area under the curve (AUC) was calculated per virus.
- Virus episodes were defined as ≥2 consecutive positive tests with a negative test pre and post. A single positive test was defined as a blip.
- We used Cox regression to evaluate the association of each virus' time-dependent and day 100 AUC with overall mortality at day 100 and day 100 through day 365.
- Logistic regression was used to identify risk factors associated with persistent virus episodes.

### Conclusions

- We demonstrate that dsDNA virus AUC through day 100 post-HCT is independently associated with overall mortality through day 365.
- Non-blip episodes have greater mean viral load and duration. Thus, non-blip episodes have higher AUCs.
- Higher viral load at time of first positive was significantly associated with progression to a non-blip episode for all viruses.
- Strategies to prevent or mitigate non-blip episodes (e.g. prophylactic medications, T-cell immunotherapy, vaccines) may improve post-HCT outcomes.

## Results

### Association of Virus AUC with Overall Mortality

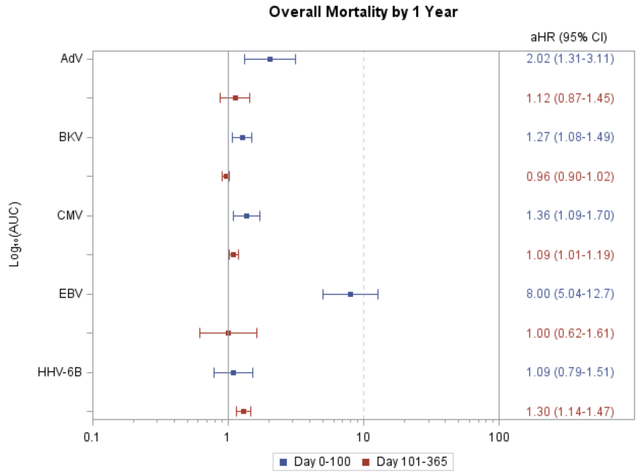


**Figure 1. Forest plot of the association of average virus area under the curve (AUC) with overall mortality through day 365 post-HCT**
We calculated the average AUC on a log10 copies/ml scale for each virus per patient by summing quantitative PCR results and dividing by the number of days followed. Virus AUC was incorporated as a time-dependent variable through day 100 (blue/top), then as a time-invariant variable through day 365 (because testing ended at day 100 [red/bottom]). All models were adjusted for age, acute GVHD, HCT comorbidity index, myeloablative conditioning, and high risk underlying disease.

### Number of Blip and Non-Blip Episodes per Virus

| Virus | Episode no., total (blips, non-blips) |
|---|---|
| CMV | 533 (223, 310) |
| BKV | 270 (67, 203) |
| HHV-6B | 206 (120, 86) |
| AdV | 44 (27, 17) |
| EBV | 46 (23, 23) |

### Mean Plasma Viral Load by Episode Duration

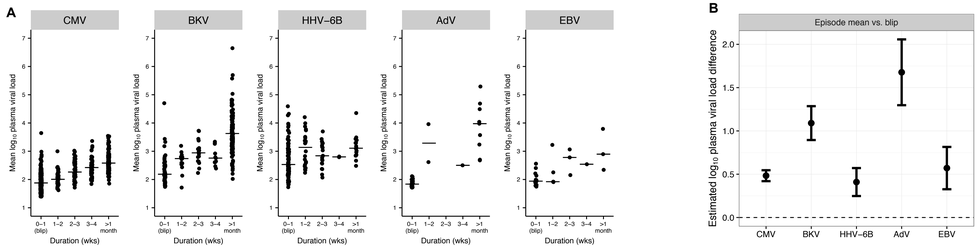


**Figure 2. A)** Each dot represents a blip or the mean viral load of an episode of the specified duration. Longer duration of viral detection is associated with higher mean plasma viral loads. Horizontal bars represent the median viral load.
**B)** Results from a linear mixed model comparing plasma viral load magnitude in blips to mean viral load magnitude in episodes. Dots represent estimated mean difference (episode - blip) and bars represent estimated the 95% CI of the mean estimate. The horizontal dotted line denotes no difference and CI's not crossing the line indicate statistical significance at the 0.05 level; all comparisons were statistically significant.

### Virologic Features of Episodes

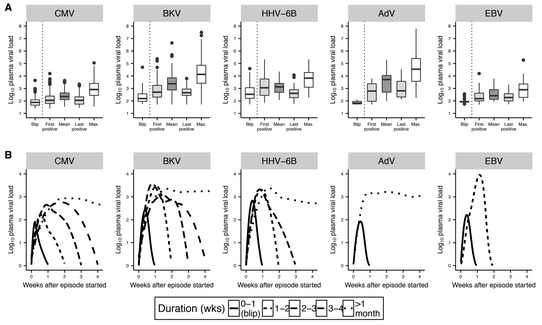


**Figure 3.** A) Virologic features of blip (single positive test) to non-blip episodes.
B) Spline-estimated trajectories for each virus by episode duration.

### Risk Factors for Progression to Non-Blip Episode

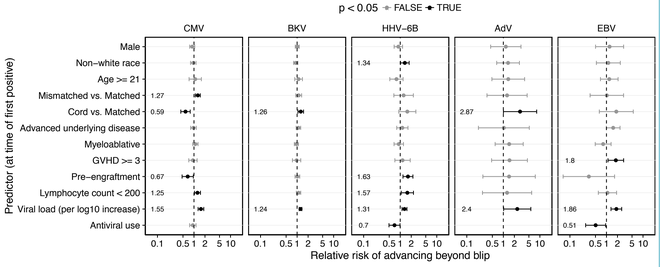


**Figure 4.** We used logistic regression with generalized estimating equations to estimate the association of each characteristic with risk of developing an episode *at the time of the first positive test*. All covariates were included in a multivariable model. Dots represent the relative risk and error bars represent the 95% CI; bolded bars were statistically significant.