

HCT recipients from 1992-2015 with lower respiratory tract disease (LRTD). Whether these findings remain pertinent in contemporary patients, the additive value of testing for viral gene transcription, and the correlation of HHV-6 detection in blood and BALF, are unknown.

Methods. We conducted a prospective study of allogeneic HCT recipients undergoing BAL for LRTD within 120 days of HCT at three cancer centers from 2015-2019. We collected and tested paired blood and BALF for HHV-6B DNA by qPCR and HHV-6B mRNA (U38 and U90 gene transcripts) among DNA positive samples using RT-qPCR. We described the detection of HHV-6B DNA and mRNA in blood and BALF, generated receiver operating characteristic (ROC) curves to determine the ability of BALF HHV-6B DNA detection to predict HHV-6B mRNA detection, and analyzed the association of HHV-6B DNA detection with mortality.

Results. We enrolled 116 allogeneic HCT recipients who underwent 125 BALs. HHV-6B DNA was detected in 45 of 122 BALF (37%) compared to 19 of 124 (15%) plasma samples. Among the 45 BALF samples with HHV-6B DNA detected, either HHV-6B mRNA transcript was detected in 22 (49%) (Figure 1). BALF HHV-6B DNA ≥ 218 copies/ml had an area under the curve of 0.93 for predicting detection of BALF viral mRNA (Figure 2). In turn, patients with BALF HHV-6B DNA ≥ 218 copies/mL had increased risk for mortality and death due to LRTD within 60 days after the BAL (Figure 3). This association remained after adjustment for age, oxygen use, and steroid use at the time of BAL in a multivariable Cox model (Figure 3).

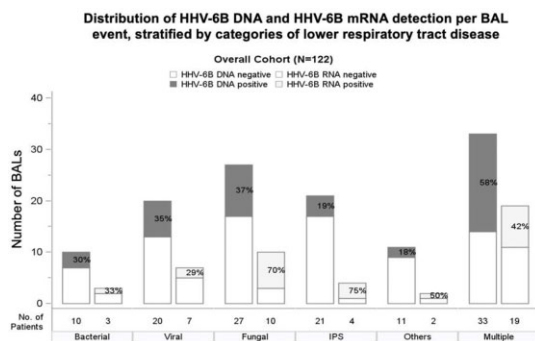


Figure 1. The X-axis indicates the clinical diagnosis category associated with each bronchoalveolar lavage (BAL) episode. The Y-axis indicates the absolute number of BALs. The first bar in each category indicates the proportion of BALs with HHV-6B DNA detection; the second bar indicates the proportion with HHV-6B mRNA detection among those with HHV-6B DNA detection.

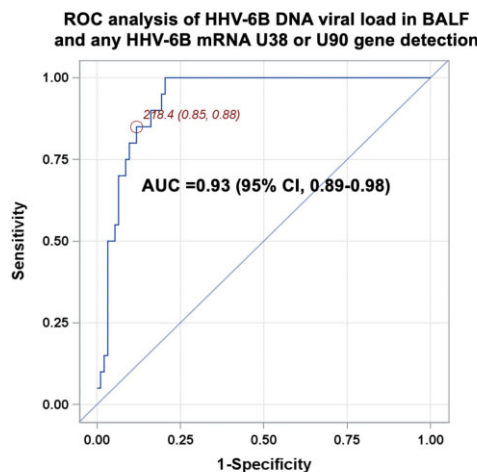


Figure 2. HHV-6B DNA ≥ 218 copies/mL in BALF maximizes sensitivity (85%) and specificity (88%) for the detection of HHV-6B U38 and/or U90 mRNA in BALF.

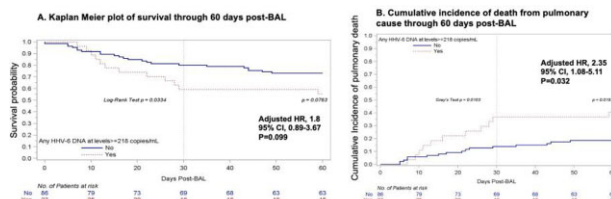


Figure 3. Adjusted hazard ratios (HR) are from multivariable Cox models adjusted for age, oxygen use (>2 liters by nasal cannula), and steroid use at the time of the BAL.

Abstract citation ID: ofac492.1716

2094. A prospective multicenter study of HHV-6B genomic DNA and gene transcription in paired bronchoalveolar lavage fluid and blood from HCT recipients

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Session: 234. Infections in Immunocompromised Individuals
Saturday, October 22, 2022: 12:15 PM

Background. We previously demonstrated frequent detection of HHV-6B DNA in bronchoalveolar lavage fluid (BALF) and its positive association with mortality in

Conclusion. HHV-6B was detected more frequently in BALF than plasma, suggesting compartment-specific reactivation. BALF HHV-6B DNA ≥ 218 copies/mL

had high sensitivity and specificity for detection of viral gene transcription in BALF and was associated with increased mortality; this viral load is strikingly similar to the BALF viral load threshold of 251 copies/mL associated with mortality in our prior retrospective study. Together, these data suggest transcriptionally active HHV-6B is a clinically impactful pulmonary pathogen in contemporary HCT recipients.

Disclosures. **Joshua A. Hill, MD**, Allovir: Advisor/Consultant|Allovir: Grant/Research Support|Covance/CSL: Advisor/Consultant|CRISPR: Advisor/Consultant|Deverra: Grant/Research Support|Gilead: Grant/Research Support|Karius: Advisor/Consultant|Karius: Grant/Research Support|Merck: Grant/Research Support|Octapharma: Advisor/Consultant|OptumHealth: Advisor/Consultant|Oxford Immunotec: Grant/Research Support|Pfizer: Advisor/Consultant|Symbio: Advisor/Consultant|Takeda: Advisor/Consultant **Alpana waghmare, MD**, Allovir: Grant/Research Support|Ansun BioPharma: Grant/Research Support|Kyorin Pharmaceutical: Advisor/Consultant|Pfizer: Grant/Research Support|Vir/GSK: Grant/Research Support **Geoffrey Hill, M.D., FRACP, FRCPA**, Applied Molecular Transport: Grant/Research Support|Compass Therapeutics: Grant/Research Support|Generon Corporation: Advisor/Consultant|Heat Biologics: Grant/Research Support|iTeos Therapeutics: Advisor/Consultant|iTeos Therapeutics: Grant/Research Support|Laevoroc Oncology: Grant/Research Support|NapaJen Pharma: Advisor/Consultant|Neoleukin Therapeutics: Advisor/Consultant|Serplus Technology: Grant/Research Support|Syndax Pharmaceuticals: Grant/Research Support **Danielle M. Zerr, MD MPH**, AlloVir: Advisor/Consultant **Sanjeet S. Dadwal, MD, FACP, FIDSA**, AlloVir: Advisor/Consultant|AlloVir: Grant/Research Support|Ansun Biopharma: Grant/Research Support|Aseptiscope: Advisor/Consultant|Aseptiscope: Stocks/Bonds|Astellas: Speaker's Bureau|Cidara: Advisor/Consultant|Gilead: Grant/Research Support|Karius: Grant/Research Support|Merck: Advisor/Consultant|Merck: Grant/Research Support|Merck: Speaker's Bureau|Takeda: Speaker's Bureau **Michael J. Boeckh, MD PhD**, Allovir: Advisor/Consultant|Amazon: Grant/Research Support|Ansun Biopharma: Grant/Research Support|EvrystBio: Advisor/Consultant|Gates Ventures: Grant/Research Support|Gilead Sciences: Advisor/Consultant|Gilead Sciences: Grant/Research Support|GlaxoSmithKline: Advisor/Consultant|GlaxoSmithKline: Grant/Research Support|Helocyte: Advisor/Consultant|Janssen: Advisor/Consultant|Janssen: Grant/Research Support|Kyorin Pharmaceuticals: Advisor/Consultant|Merck: Advisor/Consultant|Merck: Grant/Research Support|Moderna: Advisor/Consultant|Moderna: Grant/Research Support|Regeneron: Grant/Research Support|ReViral: Advisor/Consultant|Symbio: Advisor/Consultant|Takeda: Grant/Research Support|Vir Biotechnology: Advisor/Consultant|Vir Biotechnology: Grant/Research Support.