

with a mismatch in donor-recipient inherited ciHHV-6 status had increased risk for aGVHD grades 2–4 (Table 1). Identifying the impact of dual positivity for inherited ciHHV-6 on outcomes was limited by small numbers.

Conclusions: This is the largest study of outcomes after HCT with donors or recipients harboring inherited ciHHV-6. These patients did not have statistically significant differences in overall survival compared to HCT pairs without inherited ciHHV-6. Donor-recipient mismatch in inherited ciHHV-6 status increased risk for aGVHD grades 2–4. Further studies are needed to validate these findings and identify potential mechanisms leading to alloreactivity.

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Impact of Respiratory Virus Infection before Hematopoietic Cell Transplantation (HCT) on Post-Transplant Outcomes in Adults in the PCR Era: Do Rhinovirus and Coronavirus Infections Matter?

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Background: Pre-transplant respiratory virus infection has been shown to have negative impact on HCT outcomes even with human rhinoviruses (HRV) alone (Clin Inf Dis 61:192, 2015); however, the sample size was too small to separately analyze HRV and human coronaviruses (HCoV), the two most commonly diagnosed respiratory viruses. This study was performed to revisit this question in a large cohort of HCT recipients who had PCR testing for evaluation of respiratory symptoms before HCT.

Methods: Adult patients transplanted from 3/2010 to 3/2016 were retrospectively reviewed and grouped into symptomatic patients tested for respiratory virus infection within <90 days prior to transplant, and asymptomatic patients who were not tested. Viruses were categorized into four groups: adenoviruses, RSV, influenza viruses, and human metapneumovirus (HMPV) (group 1); parainfluenza viruses (PIV) 1–4 (group 2); HRV (group 3); and HCoV (group 4). HCT was delayed when feasible for groups 1 and 2 but HCT was not routinely delayed for groups 3 and 4. Transplant outcomes included “days alive and out of hospital” in allograft recipients and overall mortality by day 100 post HCT in all and allograft recipients; endpoints were analyzed using linear and Cox regression models.

Results: A total of 1,643 adult HCT recipients were included, of which 946 (58%) were allogeneic HCT recipients. Of 704 (43%) tested, 307 (44%) had pre-HCT respiratory virus infection. Group 3 viruses were most commonly detected (25%), followed by group 1, group 2, and group 4 (8% vs. 6% vs. 5%). Overall, 6% of all patients died by day 100 with no significant difference between tested and not-tested groups ($P = .84$). Among allogeneic recipients, 155 had positive detection with a median last positive day prior to HCT of –25 (IQR, –42 to –15); for mortality, 7% (42/564) died in the tested

group and 10% (37/382) died in the not-tested group ($P = .22$). In univariable analyses, pre-HCT respiratory virus infection did not negatively impact mortality in all patients and in the allogeneic HCT subset. Among, allogeneic HCT recipients, pre-HCT respiratory virus infection of individual viral groups also did not show a negative impact on days alive and out of hospital (mean difference to asymptomatic/not-tested patients: PCR positive symptomatic –1.8, 95% CI, –6.1 to 2.5; PCR negative symptomatic –3.2, 95% CI, –6.9 to .5). Results remained non-significant after adjusting for other significant risk factors (stem cell source and conditioning regimen). **Conclusion:** This study suggests that current recommendations to delay HCT for RSV, HMPV, influenza, adenovirus and PIV are effective. The presence of pre-transplant HRV and HCoV, for which delay is not routinely recommended, may not have a negative impact on transplant outcome in adult HCT recipients. Further data are needed to define the relative significance of upper versus lower respiratory tract viral infections.

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Maribavir for Treatment of Cytomegalovirus Infections Resistant or Refractory to Ganciclovir or Foscarnet in Hematopoietic Stem Cell Transplant or Solid Organ Transplant Recipients: A Randomized, Dose-Ranging, Double-Blind, Phase 2 Study

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Background: Cytomegalovirus (CMV) infection resistant or refractory to prior therapy, is common among hematopoietic stem cell transplant (SCT) and solid organ transplant (SOT) recipients and is associated with substantial morbidity and mortality among transplant recipients. Approved anti-CMV therapies are associated with adverse effects including myelosuppression, nephrotoxicity, and electrolyte imbalances. Maribavir (MBV) is active *in vitro* against CMV strains resistant to other agents. This Phase 2 study (NCT01611974) assessed the safety, tolerability, and antiviral activity of MBV for treatment of resistant or refractory CMV infections among SCT and SOT recipients.

Methods: SCT and SOT recipients aged ≥ 12 years with CMV infection (≥ 1000 DNA copies/mL in blood/plasma) resistant or refractory to (val)ganciclovir or foscarnet were randomized 1:1:1 to receive oral MBV 400, 800, or 1200 mg twice daily (BID), for up to 24 weeks. Primary safety analysis focused on incidence of treatment-emergent adverse events (TEAEs). Primary efficacy endpoint was the proportion of patients with confirmed undetectable plasma CMV DNA within 6 weeks' treatment. Secondary endpoints included the proportion of patients with plasma CMV DNA recurrence during the study.

Results: From July 2012 to December 2014, 120 patients were randomized (47 SCT, 73 SOT; 40/dose group); median age 55 (range 18–74) years. At baseline (prior to MBV therapy), 17/106 (16%) patients had neutropenia (ANC <1000/mm³). Efficacy results are shown in the table.