2648. Terminating the Tumor of Transplantation: Letermovir for Cytomegalovirus Prophylaxis
Jason Hedvat, PharmD; Patrick Lake, PharmD, BCP; Siddharth Swamy, PharmD, BCP, BCIDP; Juliana Zacchia, PharmD, BCOP; Maribel Pereiras, PharmD, BCPS, BCOP; Rami Sebit, MD; Hackensack University Medical Center, Tenafly, New Jersey; Ernest Mario School of Pharmacy, Rutgers University/Hackensack University Medical Center, Jersey City, New Jersey; John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, New Jersey

Session: 272. Studies of Treatment and Prevention of Viral Disease Saturday, October 5, 2019: 12:15 PM

Background: Letermovir is a novel antiviral that was approved for cytomegalovirus (CMV) prophylaxis after allogeneic hematopoietic stem cell transplant (allo-HSCT). The objective was to assess the real-world outcomes of CMV prophylaxis with letermovir compared with preemptive therapy (PT) alone.

Methods: This retrospective pre- and post-study evaluated the clinical impact of using letermovir prophylaxis in CMV-seropositive allo-HSCT recipients at our institution. The electronic medical record was used to identify patients that received PT alone from July 2016 to November 2017 and letermovir prophylaxis from November 2017 to March 2019. The primary endpoint was the proportion of patients with CMV infection requiring PT through week 24 after transplant. Secondary endpoints included the proportion of patients with CMV infection requiring PT through week 14 after transplant, time to CMV infection requiring PT, incidence of CMV disease, CMV-related hospitalization and all-cause mortality through week 14 and 24 after transplant. Safety data included incidence and time to engraftment and adverse effects due to letermovir. Chi-squared and t-test were utilized for categorical and continuous data respectively.

Results: The baseline characteristics were similar (Table 1) and 78.7% of patients were high risk for CMV. Fewer patients in the letermovir group (n = 58) than in the historic control group (n = 100) had CMV infection requiring PT through week 24 after transplant (18% vs. 63%, P < 0.001). The mean time to CMV infection requiring PT through week 24 after transplant was 28–161 days in the letermovir group vs. 37.4 days (11–126) in the historic control group (P < 0.001). The all-cause mortality and incidence of CMV-related hospitalization were not statistically different between the two groups (Table 2). The incidence and time to engraftment were not statistically different between the two groups (Table 3).

Conclusion: Letermovir prophylaxis in the real-world setting resulted in less CMV infection requiring PT when compared with a historic control of patients receiving PT alone. The majority of patients in the letermovir group experienced delayed-onset CMV reactivation. Letermovir was well-tolerated with no apparent myelosuppressive toxicities.

Table 1: Baseline Characteristics

Table 2: Primary and Secondary Endpoints

Table 3: Safety Endpoints

Disclosures. All authors: No reported disclosures.

2649. Measles-Containing Vaccination Resulted in a Balanced Cytokine Profile Without Evidence of Immunosuppression in Healthy 12-Month-Old Children Hayley Gans, MD; Wenqi Wang, PhD; Yael Rosenberg, Hasson, PhD; Dasseny Zerbo, PhD; Sharareh Haradadi, MPhD; Nicola Klein, MD, PhD; Stanford University Medical Center, Stanford, California; Kaiser Permanente Vaccine Study Center, Oakland, California; Kaiser Permanente Northern California, Oakland, California; National Institute of Health, Bethesda, Maryland

Session: 272. Studies of Treatment and Prevention of Viral Disease Saturday, October 5, 2019: 12:15 PM

Background: Measles virus infection results in immune activation, viral clearance and lifelong immunity. In addition, there is an immunosuppressive state defined by type 2 skewing of CD4+ T-cell cytokine production and induction of regulatory T cells with reduced dendritic cell (DC) activation in the recovery phase. Studies following measles immunization show conflicting immune profiles. To more robustly interrogate and define specific functional cytokine profiles, this study evaluated cytokine profiles in 12-month old infants before and after primary MMR vaccination.

Methods: Cytokine profiles using luminex assay (62-plex; eBioscience) were measured in 65 infants before and 42 days after MMR vaccination administered at 12 months of age as part of a randomized clinical trial. Mean cytokine percentages of children with increased or decreased concentrations of each cytokine in the post sample compared with the levels in the pre sample were evaluated using Student’s t-test. Cytokines were arranged into dominant CD4+ T-cell type, Th1, Th2, and T regulatory (Treg) and those produced by DC.

Results: No dominant cytokine pattern emerged following measles immunization, with a balanced profile. The mean percentage of children with increased and decreased concentrations (pg/mL) of signature CD4+ T-cell Th1 (tumor necrosis factor alpha [TNFa], interferon gamma [IFNg]), Th2 (Interleukin [IL] IL5, IL4, IL13), Treg (IL10, transforming growth factor-β [TGFβ]) and DC (IL12p40 and IL12p70) cytokines were equivalent when measured at 42 days after MMR vaccine compared with levels before vaccination (Table 1). (P ≥ 0.05 for all comparisons).

Conclusion: In contrast to data demonstrating an immune suppression profile following measles disease, measles-containing vaccine did not suppress Th1 CD4+ T-cell and DC cytokines or promote Th2 or Treg CD4+ T-cell cytokines measured 42 days after vaccination. The cytokine profile represents one of balance and homeostasis. This study supports the data that show measles vaccine does not cause immunosuppression in healthy infants.

Table 1. Cytokine Profile Following Measles-containing Vaccination in 12-month-old Infants

Table 2. Proportion of patients with CMV infection requiring PT

Table 3. Proportion of patients with CMV infection requiring PT

Disclosures. All authors: No reported disclosures.

2650. Evaluating Antiviral Agents for Human Noroviruses Using a Human Intestinal Enteroid Model Nicholas W. Cortes-Penfield, MD; Sasirekha Ramani, PhD; Frederick Neill, MA; Khalid Etayehi, PhD; Robert Almar, MD; Mary Estes, PhD; University of Nebraska Medical Center, Omaha, Texas; Baylor College of Medicine, Houston, Texas

Session: 272. Studies of Treatment and Prevention of Viral Disease Saturday, October 5, 2019: 12:15 PM

Background: Noroviruses are highly prevalent, worldwide, and implicated in a wide range of disease states. Though antiviral agents are being developed, no treatments are yet available. An in vitro human intestinal enteroid model was developed to evaluate potential norovirus drugs.

Methods: Human intestinal enteroids were differentiated and infected with norovirus. Cytotoxicity and cytokine expression of infected enteroids were measured to assess protective effects of potential antiviral agents. Enteroids were differentiated by inducing crypt cells to form a pseudostratified columnar epithelium. A human terminal ileum enteroid cell line was infected with norovirus and then exposed to different antiviral agents. Cytotoxicity was measured using the mitotic index and cytokine expression was analyzed using the Lumingen kit.

Results: The enteroid model showed promise in identifying potential antiviral agents. Cytotoxicity and cytokine expression were significantly reduced in enteroids treated with the antiviral agent compared to untreated enteroids. The enteroid model was able to identify potential antiviral agents that could be further developed for clinical use.

Conclusion: The enteroid model is a promising tool for evaluating potential antiviral agents for human noroviruses. Further research is needed to confirm the results and develop effective treatments for norovirus infections.

Disclosures. All authors: No reported disclosures.
Background: Norovirus can cause chronic infections with serious morbidity and mortality in immunocompromised patients. While there are no FDA-approved medications for these infections, nitazoxanide, rifabutin, and enterally administered pooled immunoglobulin (IVIG) are used off-label on the basis of expert opinion. Nitazoxanide and rifabutin show antiviral activity in a murine norovirus infection model and an in vitro deoxyribonucleic acid (DNA) transfection model of genotype GI human norovirus RNA expression, respectively. However, these drugs have not been evaluated in vivo in infections with GI4 human noroviruses, responsible for most human norovirus disease. We used the stem cell-derived nontransformed human intestinal enteroïd (HIE) system, which supports GI4 human norovirus replication, to evaluate the antiviral activities of nitazoxanide, rifabutin, and IVIG.

Methods: We inoculated HIEs with GI4 human norovirus in the presence of half-log dilutions of nitazoxanide (3 μM to 100 μM), rifabutin (10 μM to 10 mM), or IVIG (1:100 to 1:13,000) and a media control. One and 48 hours after inoculation, we extracted and quantified GI4 norovirus RNA from the HIEs. To demonstrate that replication inhibition was not due to cytotoxicity, we performed quantitative lactate dehydrogenase release assays on the HIEs across the therapeutic range of each compound.

Results: Nitazoxanide reduced GI4 replication at 48 hours in a dose-dependent manner, achieving a >90% reduction in viral replication at 10 μM without cytotoxicity. These findings were confirmed in multiple HIE lines representing different intestinal stem cells established from different donors. IVIG completely inhibited GI4 replication at up to a 1:1,000 dilution and was not cytotoxic at therapeutic concentrations. Rifabutin did not reduce GI4 replication at concentrations up to 10 mM, in excess of levels achieved in human sera with standard doses.

Conclusion: Nitazoxanide and IVIG, but not rifabutin, potently inhibit GI4 human norovirus replication in a biologically relevant in vitro model of human norovirus infection. These data highlight the use of HIEs as a new pre-clinical model for developing therapeutics for human norovirus disease.

Disclosures. All authors: No reported disclosures.

2653. Epidemiology and Risk Factors for Healthcare-Associated Viral Infections in Children

Samantha E. Hanley, BS; Folosea Odienyi, MPH; Kristin Freeman, MD, MSHP; Susan E. Cotin, MD, MPH; Julia S. Sammons, MD, MSCE; Children's Hospital of Philadelphia, Philadelphia, Pennsylvania; Philadelphia Department of Public Health, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania

Session: 272. Studies of Treatment and Prevention of Viral Disease Saturday, October 5, 2019: 12:15 PM

Background: Healthcare-associated viral infections (HA-VI) are common in hospitalized children and are increasingly recognized as a cause of preventable harm. Yet, epidemiology and modifiable risk factors related to pediatric HA-VI are currently poorly understood.

Methods: We performed a prospective case–control study to identify the risk factors of HA-VIs in children associated with pediatric HA-VI at a tertiary care children's hospital between November 2016 and August 2018. Prospective surveillance for HA-VI was performed hospital-wide by certified infection preventionists using NHSSN definitions. Cases were matched 1:1 to controls by age, duration of hospitalization, and hospital unit. We abstracted data from the electronic medical record and conducted semistructured interviews with involved caregivers to identify potential exposures beginning 4 days prior to HA-VI identification date. We also measured length of antibiotic therapy (LOT) in the 7 days following enrollment.

Results: During the study period, we identified 143 eligible patients with HA-VIs and enrolled 64 matched case–control pairs. In total, 79 viruses were identified among 64 case patients, of which 53 (67.1%) were respiratory viruses and 26 (32.9%) were GI. Case patients were more frequently exposed to a sick visitor, specifically either caregiver or sibling, compared with controls (18.8% vs. 9.4%; P = 0.26, Fisher exact test). During exposure periods, patients also had a significantly higher number of hospital procedures performed when compared with controls (n = 320 vs. 232; X² = 58.43, P < 0.001). Case, when compared with control, patients had a greater average LOT (2.89 vs. 1.08).

Conclusion: Results of study show that exposure to a sick visitor is a potentially modifiable risk factor for pediatric HA-VI. In addition, hospitalized children with HA-VI have increased exposure to antibiotic antibacterials when compared with matched controls. Prevention of pediatric HA-VI may have implications for antibiotic stewardship. Our findings suggest that hospital policies may need to be revised, with emphasis on visitor screening and partnership with families, to reduce the incidence of pediatric HA-VI during hospitalization.

Disclosures. All authors: No reported disclosures.

2654. Myocarditis in Dengue: A Prospective Observational Study

Manish Soneja, MD Medicine; Manasvini Bhatt, MBBS; Faraz A Farouqui, MD Medicine; Naval K Vikram, MD Medicine; Ashutosh Baweja, MD Medicine; Parag Khatri, MD Medicine; DM Cardiology; Navnet Vieg, MD Medicine; All India Institute of Medical Sciences, New Delhi, India

Session: 272. Studies of Treatment and Prevention of Viral Disease Saturday, October 5, 2019: 12:15 PM

Background: Cardiac involvement in dengue fever is underdiagnosed due to low index of suspicion and overlapping clinical manifestations of capillary leak associated with dengue. The frequency of subclinical dengue myocarditis and its relative contribution to the hemodynamic instability in severe dengue needs to be explored. We studied the prevalence of myocarditis and clinical outcomes among admitted patients with dengue.

Methods: A prospective observational study was carried out in admitted patients with age between 18 and 65 years having confirmed dengue (NS1/ IgM ELISA). Patients with electrolyte abnormalities or on medications affecting heart rhythm, rate,