Truncating the duration of empiric prophylactic antibiotics reduces unnecessary antibiotic use.

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

1583. The Utility of the Immunodeficiency Scoring Index (ISI) to Predict Outcomes of Coronavirus (HCoV) Infections in Hematopietic Cell Transplant (HCT) Recipients

Fareed Khawaja, MD[1]; Terri Lynn Shigle, PharmD, BCPS, BCOP[2]; Shashank S. Ghantoji, MD, PhD, MPH[3]; Marjorie Batista, MD, PhD[4]; Ella Ariza-Heredia, MD[4] and Roy F. Chemaly, MD, MPH, FIDSA, FACP[5]; [1]Department of Infectious Diseases, The University of Texas Health Science Center at Houston, Houston, Texas, [2]Division of Pharmacy, The University of Texas MD Anderson Cancer Center, Houston, Texas, [3]Infectious Diseases, The University of Texas MD Anderson Cancer Center, Houston, Texas, [4]The University of Texas MD Anderson Cancer Center, Houston, Texas, [5]Department of Infectious Diseases, Infection Control & Employee Health, The University of Texas MD Anderson Cancer Center, Houston, Texas

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Background. Respiratory viral infections in HCT recipients are associated with high morbidity and mortality, especially after progression from upper respiratory tract infection (URI) to lower respiratory tract infections (LRI). Data on risk factors (RF) for LRI and mortality is lacking for HCoV infections after HCT. We aimed to validate our ISI in HCoV infections.

Methods. All adult HCT recipients with HCoV infection from 2015 to 2017 were evaluated. An ISI based on RF was used to classify patients as low (0–2), moderate (3–6), or high (7 or higher) risk for progression to LRI or death. We defined LRI as HCoV detected in nasal wash and/or bronchoalveolar lavage and new lung infiltrates on diagnostic imaging. Clinical parameters were collected and ISI were calculated for comparison.

Results. A total of 144 adult HCT recipients with 166 episodes of HCoV infections were analyzed. The most common HCoV serotype for LRI and URI was 229E (42.4%) and OC43 (37.6%), respectively, and most patients were infected between November and March each year (Figures 1 and 2). When compared with URI, patients with LRI were more likely in the pre-engraftment period, had multiple respiratory viruses infections, had nosocomially acquired HCoV, required hospitalization, ICU transfer, and mechanical ventilation (all, $P < 0.05$). Overall mortality rate was 4% at Day 30 from diagnosis and all patients who died had LRI with an 18% mortality. Among those who died, 33% had nosocomial infection, 67% were co-infected with another respiratory virus and 67% required mechanical ventilation. Using an ISI cut off of <4, the negative predictive value (NPV) for progression to LRI was 86% with a specificity of 76%.

Conclusion. HCT recipients with HCoV LRI were more likely to have a fatal outcome. The NPV of the ISI for progression to LRI was high and could be used as a prognostic tool for future studies and for therapeutic clinical trials.

Figure 1. The seasonal distribution of HCT recipients by month of diagnosis and human coronavirus serotypes for upper respiratory infections (URIs).

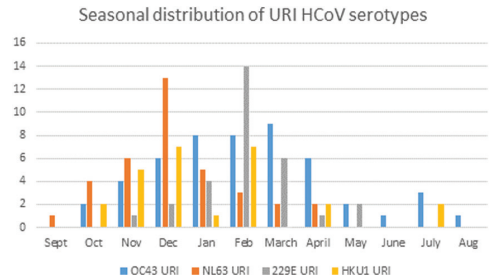
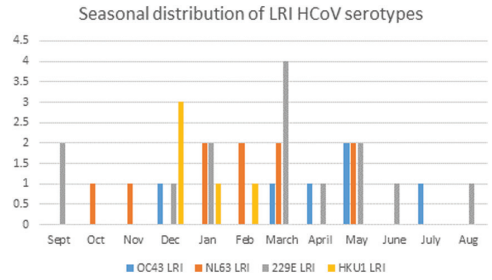


Figure 2. The seasonal distribution of HCT recipients by month of diagnosis and human coronavirus serotypes for lower respiratory infections (LRI).



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

1584. Development and Dynamics of Cytomegalovirus UL97 Ganciclovir Resistance Mutations in Transplant Recipients Detected by Next-generation Sequencing

Isabelle Paula Lodding, MD[1]; Mette Jørgensen, PhD[1]; Marc Bennedbæk, MSc. Engineering[1]; Nikolai Kirkby, MSc[2]; Klaudia Naegele, MSc.[3]; Finn Gustafsson, MD[4]; Michael Perch, MD[5]; Allan Rasmussen, MD[6]; Henrik Sengeløv, MD[7]; Søren Schwartz Sørensen, MD[8]; Hans Hirsch, MD[3,9] and Jens D Lundgren, MD[1]; [1]Centre of Excellence for Health, Immunity and Infections (CHIP), Department of Infectious Diseases, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark, [2]Department of Clinical Microbiology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark, [3]Transplantation & Clinical Virology Division Infection Diagnostics, Department of Biomedicine, University of Basel, Basel, Switzerland, [4]Department of Cardiology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark, [5]Department of Cardiology, Section for Lung Transplantation, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark, [6]Department of Surgical Gastroenterology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark, [7]Department of Haematology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark, [8]Department of Nephrology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark, [9]Infectious Diseases & Hospital Epidemiology, University Hospital Basel, Basel, Switzerland

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Background. (Val)ganciclovir resistance mutations (GRMs) in CMV UL97 (UL97-GCV-R) complicate prophylaxis and therapy of solid-organ transplant (SOT) and hematopoietic (stem) cell transplant (HCT) recipients, but data on prevalence and dynamics are scarce. We investigated UL97-GCV-R using next-generation sequencing (NGS) in transplant recipients with refractory CMV DNAemia episodes and a control group.

Methods. Between January 1, 2010–July 16, 2016, 385 transplant recipients were screened for plasma CMV DNAemia. Eighty-seven patients (54 SOT, 33 HCT) with available plasma samples had refractory CMV replication at viral loads ≥910 IU/mL and were analysed by NGS. If UL97-GCV-R were detected in >10% of the NGS reads, all earlier plasma samples were also analysed by NGS. For comparison, this approach was also performed in a control group of 21 patients (14 SOT, 7 HSCT) with DNAemia episodes resolving under antiviral therapy. UL97-targeted NGS was performed using Illumina MiSeq and analysed by LoFreq for variant calling.

Results. Of the 87 recipients with refractory CMV replication, 19 (22%) had ≥1 UL97-GCV-R detected by NGS (Table 1, Figure 1), in comparison to 0/21 (0%) of the controls ($P = 0.02$). Fourteen of 19 of the resistant cases (20 induced mutations) had NGS performed <4 week from onset of infection; in this sample, the mutation was either not detected, detected as minority or dominating variant for 11, 7 and 2, respectively. In the majority of recipients one dominant mutant was induced (68%); ≥2 mutations were detected in the remaining recipients (Table 1). Most frequent UL97-GCV-R affected codon-595 (42%), -594 (32%) or -603 (32%). The % of C592G was low in in all episodes (<15%) without changing during the course (Figure 1). There was a trend toward higher frequencies of donor (D)/recipient (R) CMV high-risk mismatch, CMV disease and prior failure to valganciclovir prophylaxis (SOT) or treatment (HCT) among the cases with UL97-GCV-R (Figure 2).

Conclusion. UL97-GCV-R was seen in 22% of refractory CMV replication episodes. CMV D/R mismatch and CMV disease were more common amongst resistant cases. The C592G mutation was present in low frequency in all patients, suggesting that this mutation was part of the quasispecies, and not selected by ganciclovir resistance. Implications for clinical management will be discussed.

Table 1. Details on clinical and genotypic features of 19 transplant recipients with induced* ganciclovir resistance mutations in the CMV UL97 gene.

Patients	Tx type	CMV IgG D/R status	CMV disease	Prophylaxis or treatment failure	Codon in amino acid							Number of mutations induced/ patient
					460I or V	520Q	594V or G	595S or F	596G	603W	607Y or F	
1	MAC HCT	D-/R+	CMV GI disease	No							++ (both in same)	2
2	MAC HCT	D-/R+	CMV GI disease	No						++		1
3	MAC HCT	D-/R-	CMV Retinitis	No	++				++			2
4	MAC HCT	D-/R+	CMV GI disease	No			++	++				2
5	MAC HCT	D-/R+	No	Yes			++					1
6	NMA HCT	D-/R+	CMV GI disease	No			++					1
7	Liver	D+/R-	CMV pneumonia	Yes		++				++		2
8	Liver	D+/R-	No	Yes						++		1
9	Liver	D+/R-	No	Yes						++		1
10	Lung	D+/R-	CMV pneumonia	No				++				1
11	Lung	D+/R-	CMV GI disease	Yes				++				1
12	Kidney	D+/R-	No	Yes			++			++	++	3
13	Kidney	D+/R-	No	Yes				++				1
14	Kidney	D+/R-	No	Yes		++	++			++		3
15	Kidney	D+/R-	CMV Pneumonia	No			++ (both in same)	++				3
16	Kidney	D+/R-	No	Yes				++				1
17	Kidney	D+/R+	No	Yes				++				1
18	Kidney	D+/R-	No	Yes	++							1
19	Kidney	D+/R-	No	Yes				++				1
Number of patients with mutation					2/19	2/19	6/19	8/19	1/19	6/19	2/19	
% with mutation induced					10,5	10,5	31,6	42,1	5,3	31,6	10,5	

*Induced mutations defined as mutations with a maximum frequency ≥25%, and a minimum increase of 10% in the subsequent sample.
Abbreviations: GI; gastro-intestinal, HCT; hematopoietic stem cell transplantation, MAC; myeloablative conditioning, NMA; non-myeloablative conditioning.