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Session: 33. Transplant ID

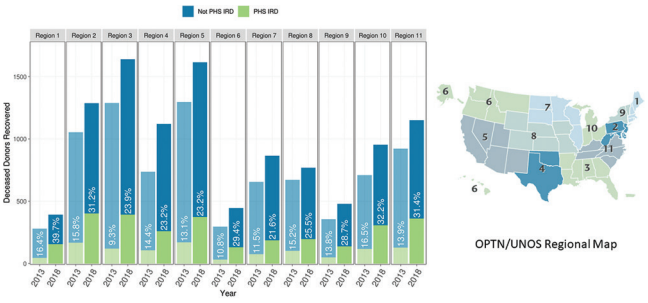
Thursday, October 3, 2019: 10:45 AM

Background. In the United States, all deceased donors (DD) are evaluated for behavioral risk factors for human immunodeficiency virus (HIV), hepatitis B (HBV), and hepatitis C (HCV) infection during the past 12 months. DD with behavioral risk factors or hemodilution are designated as PHS increased risk donors (IRD). Since 2013, the number of IRD has increased from 13.4% of DD to 27% in 2018. Despite a low residual risk of disease transmission after a negative nucleic acid test for HIV/HBV/HCV, the considerable underutilization of IRD has driven an interest in revising the PHS IRD 2013 guidelines. The objective of this study was to describe the epidemiology of IRD with the goal of guiding policy change and maximize organ use.

Methods. This is a retrospective cohort study of DD during 2018. Characteristics of IRD were compared with non-IRD. A random 10% sample of IRD was selected for manual review of text narratives and donor questionnaires submitted by organ procurement organizations to determine specific PHS IRD factors. Categorical variables were compared using the χ^2 test and continuous variables were compared using a 2-sample *t*-test for independent samples.

Results. Among 10,721 DD in 2018, 2,904 were designated IRD (27.1%) with regional variability noted (Figure). Compared with non-IRD, IRD were younger (median age 35 vs. 45 years, $P < 0.001$) and more often died from drug intoxication (33.2 vs. 5.6%, $P < 0.001$). Hemodilution was found in 6.8% of all IRD and was the only factor for IRD designation in 60% of pediatric donors <12 years old. The random sample of IRD ($N = 288$) was similar to IRD population for age, gender, ethnicity, cause of death, and region of recovery (table). Descriptive analysis of the random sample showed that intravenous drug use was the most common behavioral risk factor ($N = 124$, 43.1%), followed by incarceration ($N = 108$, 37.5%). Most DD met only 1 criterion ($N = 179$, 62%); 21% met 2 criteria; and 17% had >3 criteria.

Conclusion. This study represents the most detailed description of PHS IRD factors since the adoption of the new guidelines in 2013. Understanding the prevalence of factors that lead to IRD designation will help inform future policy development, optimize safe DD use, and increase the number of transplants.



Deceased Donors in the USA by PHS IRD Status : 2013 & 2018

Table: Deceased-Donor Demographics and PHS Risk Factors in 2018

Characteristic	All 2018 Deceased Donors	All 2018 IRD	Random Sample of 2018 IRD
Number of Donors (N)	10,721	2,904	290
Donor Age (Median, IQR)	41 (28—54)	35 (27—46)	36 (27 – 45)
Pediatric (<12 y.o.) Donors (N, %)	479 (4.5%)	47 (1.6%)	4 (1.4%)
Mechanism of Death: Drug Intoxication (N, %)	1401 (13.1%)	964 (33.2%)	92 (31.7%)
Female Donors (N, %)	4225 (39.4%)	944 (32.5%)	92 (31.7%)
Donor Ethnicity (N, %)			
White	7008 (65.4%)	1995 (68.7%)	211 (72.3%)
Black or African—American	1728 (16.1%)	458 (15.8%)	39 (13.4%)
Hispanic	1508 (14.1%)	350 (12.1%)	33 (11.4%)
Other/Multiracial	477 (4.4%)	101 (3.5%)	5 (1.7%)
PHS IRD Risk Factors (N, %)			
IVDA	---	---	124 (43.1%)
Incarceration	---	---	108 (37.5%)
Sex w/ Individual with IVDU	---	---	53 (18.4%)
Incomplete/Unclear History	---	---	37 (12.8%)
Hemodilution	197 (1.8%)	197 (6.8%)	30 (10.4%)
Hemodialysis	---	---	27 (9.4%)
Sex w/ Individual Who Had Sex for Money/Drugs	---	---	24 (8.3%)
Sex for Money/Drugs	---	---	19 (6.6%)
Dx/Rx for STI	---	---	19 (6.6%)
Sex w/ Individual Known/Susp. w/ HIV/HBV/HCV	---	---	18 (6.2%)
MSM	---	---	11 (3.8%)
Female Who had Sex with MSM	---	---	2 (0.7%)
Pediatric Donor: Born to MO w/ or Increased Risk for HIV/HBV/HCV	---	---	1 (0.3%)
Pediatric Donor: Breastfed by MO w/ or Increased Risk for HIV	---	---	0 (0%)

Disclosures. **All Authors:** No reported Disclosures.

89. Efficacy and Tolerability of Voriconazole (VOR) vs. Isavuconazole (ISA) Prophylaxis (px) in Preventing Invasive Fungal Infections (IFI) in Lung Transplant Recipients (LTR)

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Session: 33. Transplant ID

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Background. IFI is a significant complication following lung transplant (LT). VOR was universal antifungal px in our LT program from 2004 to October 2015, at which time px was changed to ISA. We compared the efficacy and tolerability of VOR vs. ISA px in LTR.

Methods. We reviewed all LTR from September 2013 to February 2018 who received VOR or ISA Px. The standard duration of px was 3 or 4 months following basiliximab and alemtuzumab induction, respectively. All patients were followed for ≥1 years post-Tx. IFI was defined by revised EORTC/MSG criteria.

Results. In total, 310 LTR were included, 149 and 161 of whom received ISA and VOR px, respectively. There was no difference in demographics, underlying diseases, single vs. double LT, or induction therapy (alemtuzumab vs. basiliximab) between the 2 groups. At 1-year after LT, 9% (14) and 8% (13) of patients in ISA and VOR groups developed IFI, respectively ($P = 0.5$). 5% (7) and 3% (5) of patients developed breakthrough (BT) IFI during ISA and VOR px, respectively ($P = 0.6$; Figure 1, $P = 0.4$, Kaplan-–Meier). ISA BT included pneumonia (PNA, 2), endobronchial IFI (2), mediastinitis (1), chest wall IFI (1), and candidemia (1). ISA BT patients were infected with *Aspergillus fumigatus* (3; 2 with ISA MIC = 0.5 µg/mL, 1 MIC = 1 µg/mL), black mould (1), and yeasts (3; 2 *C. glabrata*, 1 *C. albicans*). VOR BT IFI included PNA (2), endobronchial IFI (1), empyema (1), and chest wall IFI (1). VOR BT IFIs were due to *A. ustus*, *A. niger*, *A. lentulus*, black mould, and *Rhizopus* spp (1 each). All *Aspergillus* VOR BT isolates exhibited VOR MIC ≥2 µg/mL. Patients with IFI were more likely to have positive pre-LT respiratory fungal culture ($P = 0.01$) and grade ≥3 ischemic reperfusion injury (IRI) post-LT ($P = 0.01$). VOR and ISA were prematurely discontinued in 53% (85) and 14% (21) of patients due to adverse events, respectively ($P < 0.0001$). Hepatotoxicity was more common with VOR (22%, 35) than ISA (5%, 7) ($P < 0.0001$). IFI was an independent risk factor for death at 1 year (Figure 2, $P < 0.0001$, Kaplan–Meier).

Conclusion. ISA was as effective as VOR in preventing IFI in LTR, and significantly better tolerated. Pre-LT fungal culture positivity and grade ≥3 IRI post-LT were risk factors for the development of IFI. IFI within 1-year post-LT had a significant impact on mortality

Fig 1 - Breakthrough IFI during antifungal prophylaxis

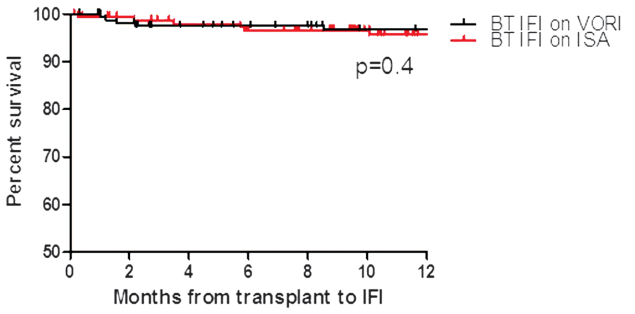
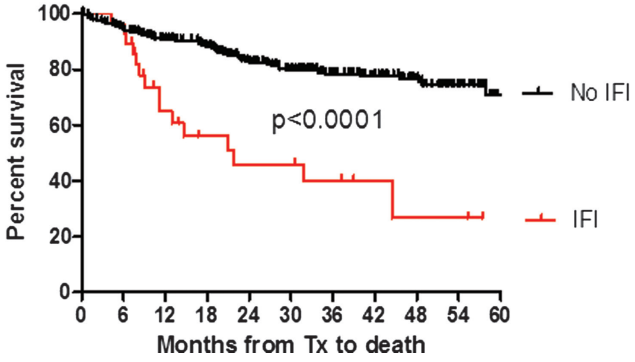


Fig 2 - Mortality of lung transplant patients



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90. Fecal Microbiota Transplantation in Metastatic Melanoma Patients Resistant to Anti-PD-1 Treatment

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Session: 33. Transplant ID

Thursday, October 3, 2019: 11:15 AM

Background. Most metastatic melanoma patients treated with Programed cell Death (PD)-1 blockers fail to achieve a durable response. The gut microbiota profoundly affects host immunity, and fecal microbiota transplantations (FMT) have been shown to enhance anti-PD-1 effectiveness in murine models. We report initial safety and efficacy results from the first patients treated in a Phase I study of FMT and re-induction anti-PD-1 therapy in anti-PD-1 refractory metastatic melanoma.

Methods. FMT donors were two metastatic melanoma patients who achieved a durable complete response to treatment. FMT recipients were metastatic melanoma patients who failed at least one anti-PD-1 line of treatment. FMT was conducted by both colonoscopic and oral administration, followed by anti-PD-1 re-treatment. Each recipient underwent pre- and post-treatment stool sampling, tissue biopsy of both gut and tumor, and total body imaging.

Results. Five patients with treatment-resistant metastatic melanoma were recruited. No FMT-related or immunotherapy-related adverse events were observed. To assess engraftment of the new microbiota, recipients were paired with their respective donors and stool 16S rDNA gene sequence analysis was performed. Sequencing results demonstrated post-FMT compositional dissimilarity (Unweighted UniFrac, $P = 0.04$, FDR $q = 0.22$) between the two recipient–donor groups. Specific taxonomic dynamics included post-FMT increased abundance of *Paraprevotellaceae*, previously associated in descriptive studies with responsiveness to treatment, and significant reductions in abundance of β-proteobacteria, previously associated with reduced response to treatment. Immunohistochemical stains of biopsies demonstrated an increased post-FMT infiltration of antigen presenting cells (CD68+) in the gut (paired *T*-test, $P = 0.008$) and in the tumor ($P = 0.0076$). Post-treatment intra-tumoral CD8+ T-cell infiltration was also increased. Three patients had a partial or complete response to treatment post-FMT.

Conclusion. FMT in metastatic melanoma patients seems to be safe and may alter recipient gut microbiota to resemble that of a responder donor. This alteration may result in intra-tumoral T-cell activity, and conferred clinical and radiological benefit in several recipients previously unresponsive to treatment.

Disclosures. **All Authors:** No reported Disclosures.

91. Differential Impact of Cytomegalovirus (CMV) Donor (D) Serostatus on Rates and Kinetics of CMV Viremia among CMV Seropositive Recipients (R+) of Ex vivo T-cell Depleted (TCD) and Unmodified (CONV) Hematopoietic Cell Transplants (HCT)

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Session: 33. Transplant ID

Thursday, October 3, 2019: 11:30 AM

Background. In unmodified (CONV) HCT, CMV donor seropositivity (D+) conveys partial protection against CMV disease mediated by the transfer of donor CMV T-cell immunity through the allograft. Ex vivo T-cell depletion by CD34 selection affords a stringent depletion of donor T cells, thus transfer of donor T-cell immunity to CMV would be negligible. We evaluate the impact of CMV D serostatus on rates and kinetics of CMV viremia by Day (D)100 post-HCT in a contemporary cohort of CONV and TCD recipients from a single center.

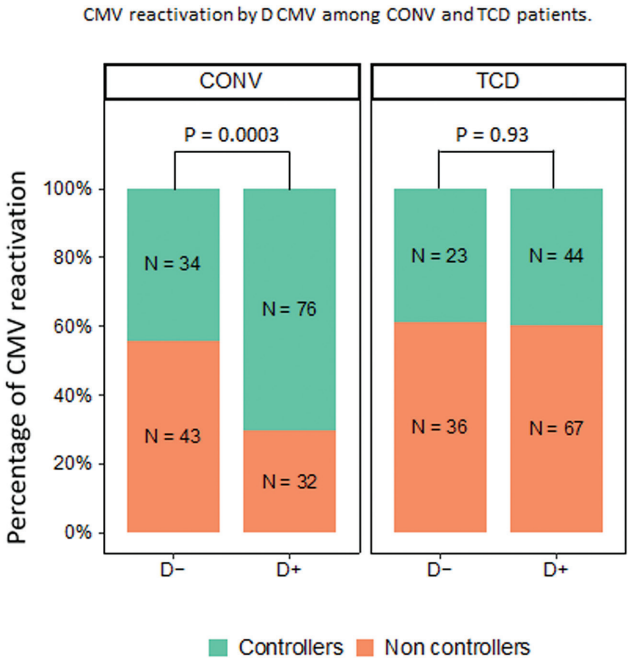
Methods. A retrospective cohort study of R+ adult recipients of first peripheral blood or marrow HCT for hematologic malignancies (excluding multiple myeloma) from June 2010 to December 2017 at MSKCC. Routine CMV monitoring by a quantitative PCR assay occurred weekly from D14 through D100. Patients were treated preemptively. CMV viral burden was assessed as the time-averaged area under the viremia curve over 100 days from HCT (AAUC) calculated as the sum of the area of trapezoids of AUC viral loads divided by the number of weeks of follow-up viremia. The median AAUC for all patients with CMV reactivation (AAUC50) was used to classify patients as CMV controllers (AAUC ≤ AAUC50) or noncontrollers (AAUC >AAUC50).

Results. Of 509 R+, 290 (57%) patients received CONV and 219 (43%) TCD HCT; from 300 (59%) D+ and 209 (41%) D− donors. In CONV, CMV viremia occurred with similar frequency in D+ (65%) and D− (62%), $P = 0.6$. In contrast, in TCD, CMV viremia occurred more frequently in D+ compared with D− (83% vs. 71%, $P = 0.03$). Among CONV, D+ was associated with lower CMV burden (median AAUC) compared with D− (0.791 vs. 1.13, respectively, $P = 0.0004$). In contrast, in TCD, AAUC was similar between D− and D+ (1.19 vs. 1.35; $P = 0.86$). Among CONV with CMV viremia, D− were more likely to be noncontrollers compared with D+ (56% vs. 31%, respectively, $P = 0.001$). In contrast, among TCD with CMV viremia the proportion of noncontrollers was similar between D− and D+ (61% vs. 60%, respectively; $P = 1$).

Conclusion. Donor CMV serostatus has a differential effect on rates and kinetics of CMV viremia in R+ TCD and CONV HCT recipients. D+ is associated with less CMV viremia and less CMV burden in CONV but not in TCD. Our findings, if confirmed, have implications for donor selection algorithms.

		All N=509	TCD N=219	%	CONV N=290	%
Gender	Female	231	105	48%	126	43%
	Male	278	114	52%	164	57%
Sero-status	D+	300	134	61%	166	57%
	D-	209	85	39%	124	43%
Underlying malignancy	Leukemia	311	156	71%	155	53%
	MDS	81	47	21%	34	12%
	Lymphoma	83	3	1%	80	28%
	Other	34	13	6%	21	7%
Donor type	MRD	176	78	36%	98	34%
	MUD	254	112	51%	142	49%
	MMRD/MMUD	79	29	13%	50	17%
Conditioning	Myeloablative	316	217	99%	99	34%
	Non-ablative	51	0	0%	51	18%
	Reduced intensity	142	2	1%	140	48%
Acute GVHD =2	Yes	179	42	19%	137	47%
	No	330	177	81%	153	53%

Table 1. Patients baseline characteristics.
TCD: T cell depleted, CONV: Conventional, D: Donor sero-status, MDS: Myelodysplastic syndrome, MRD: Matched related donor, MUD: Matched unrelated donor, MMRD: Mismatched related donor, MMUD: Mismatched related donor, GVHD: Graft versus host disease.



Disclosures. **All Authors:** No reported Disclosures.

92. Incidence of Respiratory Syncytial Virus Infection among Hospitalized Adults, 2017–2019

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Session: 34. Viral Infections - Host, Pathogen, and Impact of Intervention

Thursday, October 3, 2019: 10:30 AM

Background. Respiratory syncytial virus (RSV) infection has been increasingly recognized as an important cause of acute respiratory illness (ARI) and a trigger for exacerbation of underlying cardiopulmonary disease in adults. Incidence of hospitalized RSV infection remains uncertain as adults have not been systematically screened.