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

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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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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 \leq 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; $P = 1$).

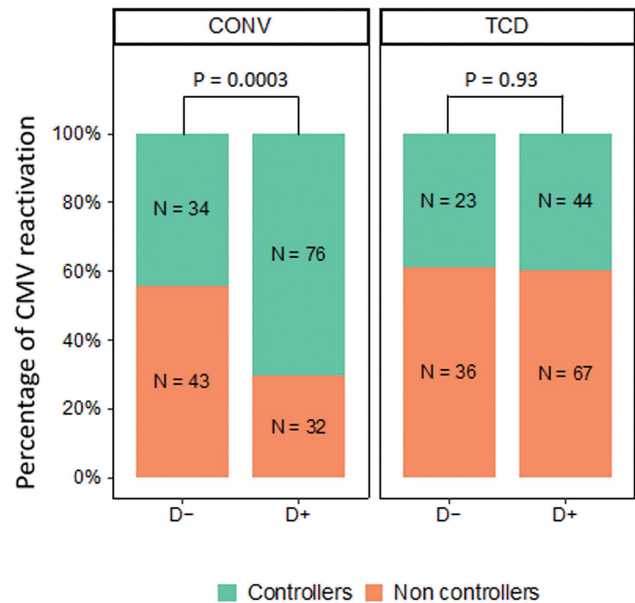
Conclusion. Donor CMV serostatus has a differential effect on rates and kinetics of CMV viremia in R+ TCD and CONV HCT recipients. D+ is associated with less CMV viremia and less CMV burden in CONV but not in TCD. Our findings, if confirmed, have implications for donor selection algorithms.

		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.

CMV reactivation by D CMV among CONV and TCD patients.



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

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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.