Conclusion: Antibiotic prophylaxis was frequently used after KP with TMP-SMX being the most common antibiotic used. Patients in the no-prophylaxis group had significantly fewer cholangitis episodes compared to those receiving antibiotic prophylaxis. Prophylactic antibiotics did not have an impact on time to LVT. Our findings suggest that antibiotic prophylaxis is not helpful in decreasing the frequency of cholangitis episodes after KP and may increase the risk for infections with resistant bacteria. Larger prospective randomized control studies are recommended.

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580. Refractory and Resistant CMV Infections in Hematopoietic Cell Transplant Recipients in the Letermovir Primary Prophylaxis Era

Joseph Sassine, MD[1]; Fareed Khawaja, MBBS[2]; Victoria Handy, PharmD[2]; Terri Lynn Shigle, PharmD[2]; Farnaz Foolad, PharmD[2]; Samuel L. Aitken, PharmD, MPH, BCIDP[3]; Samuel L. Aitken, PharmD, MPH, BCIDP[3]; Ella Ariza Heredia, MD[3]; Roy F. Chemaly, MD, MPH, FACP, FIDSA[3]; [1]University of Texas Health Science Center at Houston, Houston, Texas; [2]University of Texas MD Anderson Cancer Center, Houston, Texas; [3]The University of Texas MD Anderson Cancer Center, Houston, Texas

Session: P-22. Care Strategies for Transplant Patients

Background: CMV reactivation is one of the most common infections after allogeneic hematopoietic cell transplantation (allo-HCT) and carries considerable morbidity and mortality. Primary prophylaxis with letermovir demonstrated in clinical trials reduction of the incidence of clinically significant CMV infection (CS-CMVi). This study aims at exploring the effect of letermovir primary prophylaxis on the occurrence of refractory or resistant CMV infections.

Methods: This is a single-center, retrospective cohort study of 537 consecutive allo-HCT CMV-seropositive recipients cared for between March 2016 and December 2018. Baseline demographics, transplant characteristics, CMV infections, treatment and mortality data were collected from the electronic medical record (Table 1). CMV outcomes were defined according to the standardized definitions for clinical trials. Data was analyzed on IBM® SPSS version 24 using a logistic regression model for multivariate analysis.

Results: Out of 537 patients identified, 123 received letermovir for primary prophylaxis during the first 100 days post-HCT and 414 did not. In a multivariate analysis, primary prophylaxis with letermovir was associated with a reduction in CS-CMVi (OR 0.11, 95% CI 0.06–0.20), CMV disease (OR 0.20, 95% CI 0.08–0.46) and refractory or resistant CMV infection (OR 0.11, 95% CI 0.02–0.49) (Table 2). Notably, there was no resistant CMV and no CMV-related mortality in the letermovir group. There was a trend towards lower all-cause mortality at day 100 in the letermovir group (OR 0.48, 95% CI 0.18–1.2).

Table 1 - Baseline Characteristics.

	Letermovir (N = 123)		Non-Letermovir (N = 414)	
Gender				
Male	64	52%	215	51.9%
Female	59	48%	199	48.1%
Race				
White	79	64.2%	272	65.7%
Black	10	8.1%	29	7%
Hispanic	18	14.6%	68	16.4%
Asian	5	4.1%	18	4.3%
Middle Eastern	7	5.7%	22	5.3%
Other	4	3.3%	5	1.3%
Underlying Disease				
AML	52	42.3%	187	45.2%
ALL	16	13%	59	14.2%
MDS	14	11.4%	57	13.8%
MF	10	8.1%	33	8%
Others	31	25.2%	78	18.8%
Age at Transplant (years)				
Median (Range)	57 (18 – 73)		54 (6 – 78)	
Type of Transplant				
MRD	37	30.1%	128	30.9%
MUD	52	42.3%	189	45.6%
Haploidentical	24	19.5%	74	17.9%
Cord	4	3.2%	22	5.3%
MMUD	6	4.9%	1	0.3%
Source of Cells				
Bone Marrow *	26	21.1%	141	34%
Peripheral *	93	75.6%	251	60.7%
Cord	4	3.3%	22	5.3%
Donor CMV Status*				
Seropositive	80	65%	211	51%
Seronegative	43	35%	203	49%
Induction & GVHD prophylaxis *				
ATG-based induction	19	15.4%	134	32.4%
Post-Cyclophosphamide	78	63.4%	158	38.2%
Time to engraftment (days)				
Median (Range)	15 (7 – 124)		15 (7 – 49)	
Other prophylaxis				
Lead in ganciclovir	30	24.4%	91	22%
Foscarnet into transplant	0	0%	4	1%
No other prophylaxis	93	75.6%	321	77%
GVHD				
Any GVHD	65	52.8%	212	51.2%
GVHD within 100 days	60	48.8%	199	48.1%

* denotes statistically significant difference between the two groups

Abbreviations – AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; MDS, myelodysplastic syndrome; MF, myelofibrosis; MRD, matched related donor; MUD, matched unrelated donor; MMUD, mismatched unrelated donor; CMV, cytomegalovirus; GVHD, graft-versus-host disease; ATG, antithymocyte globulin

Table 2 - Multivariate Analysis of Clinical Outcomes.

	Letermovir (N = 123)		Non-Letermovir (N = 414)		Adjusted OR	95% CI	p-value
CS-CMVi	21	17.1%	221	53.4%	0.11	0.06-0.20	<0.001
CMV Disease	7	5.7%	83	20%	0.20	0.08-0.46	<0.001
Refractory or Resistant CMV	2	1.6%	45	10.9%	0.11	0.02-0.49	0.004
All-cause mortality at day 100	9	7.3%	52	12.6%	0.47	0.18-1.2	0.12
All-cause mortality at week 24	21	17.1%	82	19.8%	1.1	0.58-2.1	0.76
All-cause mortality at week 48	34	27.6%	130	31.4%	1.2	0.70-2.1	0.51

Conclusion: Our study showed a strong association between primary prophylaxis with letermovir and reduction in refractory or resistant CMV infections and CMV disease in allo-HCT recipients.

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581. Risks versus Benefits of Metronidazole Use for the Prevention of Acute GVHD in Allogeneic Stem Cell Transplant Recipients

Mary T. Young, PharmD[1]; Marguerite Monogue, PharmD[1]; Hetalkumari Patel, PharmD[1]; [1]University of Texas Southwestern Medical Center, Houston, Texas

Session: P-22. Care Strategies for Transplant Patients

Background: Currently, acute graft versus host disease (aGVHD) prophylaxis in hematopoietic stem cell transplants (HSCT) varies amongst different institutions. There is a lack of data supporting the use of metronidazole for aGVHD prophylaxis in HSCT. To further investigate if metronidazole has an effect on aGVHD, allogeneic HSCT recipients will be examined to determine if metronidazole post-transplantation decreases the incidence of aGVHD and the risks of adverse drug events (ADE) associated with this practice.

Methods: This retrospective study included 120 adult patients who received an allogeneic HSCT between January 1, 2010 to December 31, 2013. The primary endpoint is the incidence of aGVHD, defined as within 100 days post-transplant. Secondary endpoints include the rate of metronidazole discontinuation due to intolerance, frequency of metronidazole-related adverse effects, incidence of Clostridioides difficile infection, mortality, and overall survival.

Results: One hundred six patients met the inclusion criteria. The majority of patients received metronidazole (88 vs. 18). Less patients in the metronidazole arm developed aGHVD (51.1% vs 61.1%, p=0.44). In the subcategories of liver, skin, and gastrointestinal aGHVD, patients who received metronidazole developed less gastrointestinal aGVHD (26.1% vs 50.0%, p=0.045). Gastrointestinal ADEs were the most common metronidazole-related ADEs (19.3%, Table 1). There were no significant differences in the incidence of *C. difficile* infection, mortality, and overall survival between the two arms (Table 2).

Table 1. Adverse Drug Events and Discontinuation of Therapy

Results	Metronidazole (n = 88)
Metronidazole-related adverse effects	22 (25.0%)
Headache	0 (0%)
Gastrointestinal	17 (19.3%)
Metallic taste	3 (3.4%)
Central neurotoxicity	0 (0%)
Neuropathy	0 (0%)
Infection	0 (0%)
Other adverse effect	3 (3.4%)
Metronidazole discontinuation due to intolerance	20 (22.7%)
Metronidazole duration, as days, median (range)	32.5 (1-50)

Table 2. Additional Secondary Outcomes

Results	No metronidazole (n = 18)	Metronidazole (n = 88)	P-value
C. difficile infection	1 (5.6%)	7 (7.3%)	1.00
Mortality – GVHD-related			0.90
GVHD-related	2 (11.8%)	15 (88.2%)	--
Not GVHD-related	8 (20.0%)	32 (80.0%)	--
Unknown	1 (16.7%)	5 (83.3%)	--
Still alive	7 (16.3%)	36 (83.7%)	--
Overall survival			--
100 day	17 (17.9%)	78 (82.1%)	0.69
1 year	12 (15.8%)	64 (84.2%)	0.60

Conclusion: Despite a reduction in gastrointestinal aGVHD in the metronidazole arm, approximately one in four patients experienced an ADE to the medication, likely due to the prolonged use of the medication (33 days). The utilization of post-transplant cyclophosphamide for GVHD prophylaxis likely eliminates the need for metronidazole; however our findings suggest a benefit in preventing gastrointestinal aGVHD with metronidazole; albeit, caution is warranted given the high incidence of ADE associated with prolonged use.

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