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ABSTRACT

02853 Impact of co-administration of letermovir on isavuconazole plasma concentration in allogeneic hematopoietic cell transplant (HCT) recipients

01. Viral infection & disease (excl. COVID-19)

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Background

There is paucity of data on coadministration of isavuconazole (ICZ) with letermovir (LET) in allogeneic hematopoietic cell transplant (HCT) recipients. We compared ICZ plasma concentration (C_{trough}) in HCT recipients with and without coadministration of LET.

Methods

Retrospective review of HCT recipients who received ICZ for primary antifungal prophylaxis in an open label study from June 1, 2017 to October 31, 2018 and had ≥1 ICZ C_{trough}. ICZ started by day 9 post HCT. ICZ C_{trough} levels were checked when patients had been on a stable dose of oral ICZ for ≥ 1 week and during episodes of Gastrointestinal (GI) GVHD if patients were able to tolerate and absorb oral medications. CMV-seropositive (R+) recipients who received HCT after December 2017 received LET for CMV prevention. Patients were categorized into two groups no-LET and LET. ICZ C_{trough} were compared between groups using Mann–Whitney U tests.

Results

Of 89 patients analyzed, 20 (22%) patients received concomitant LET. Baseline characteristics were similar between no-LET and LET groups (**Figure 1**). Eighteen (20%) patients had ≥ 2 ICZ C_{trough} measured. A total of 109 ICZ C_{trough} were obtained at a median of 31 (interquartile range [IQR]: 23-41) days from HCT infusion. In LET group, ICZ C_{trough} were obtained after 16 (IQR: 2-22) days from LET initiation. The median C_{trough} was 3.0 (IQR: 2.2-4.2) µg/mL for all patients. ICZ C_{trough} were similar between no-LET and LET groups (**Figure 2**). Twenty patients with GI GVHD had 27 ICZ C_{trough}. ICZ C_{trough} were similar in patients with and without GI GVHD

(median 2.7, IQR: 1.9-3.8 µg/mL versus median 3.3, IQR: 2.5-4.2 µg/mL, respectively; p=0.089).

Conclusions

ICZ C_{trough} were within the expected range with or without LET coadministration in allogeneic HCT. Given reported decrease in C_{trough} of voriconazole during letermovir administration, isavuconazole provides an alternative azole with less drug-drug interactions and pharmacokinetic variability.

Figure 1. Comparison of baseline characteristics

Characteristics		No-LET (N = 69)	LET (N = 20)	P value
		N (%)	N (%)	
Age	Median (IQR), years	57 (51, 66)	58 (47, 64)	0.673
Gender	Male	50 (72)	11 (55)	0.139
Underlying disease	Leukemia/MDS	47 (68)	15 (75)	0.823
	Lymphoma	12 (17)	3 (15)	
	Other hematologic malignancy	10 (14)	2 (10)	
Donor type	Matched related/unrelated	45 (65)	9 (45)	0.260
	Mismatched related/unrelated	16 (23)	7 (35)	
	Haploidentical	8 (12)	4 (20)	
HCT source	Bone marrow	13 (19)	2 (10)	0.118
	Cord blood	8 (12)	6 (30)	
	Peripheral blood	48 (70)	12 (60)	
Conditioning	Myeloablative	37 (54)	10 (50)	0.775
	Reduced/ Non-myeloablative	32 (46)	10 (50)	
GvHD prophylaxis	Ex vivo T-cell depletion	23 (33)	6 (30)	0.086
	Cyclosporine + Mycophenolate Mofetil	10 (14)	6 (30)	
	Cyclophosphamide + Mycophenolate + Tacrolimus or Sirolimus	12 (17)	6 (30)	
	Tacrolimus + Mycophenolate Mofetil + Methotrexate	24 (35)	2 (10)	

Figure 2. Comparison of ICZ C_{trough}