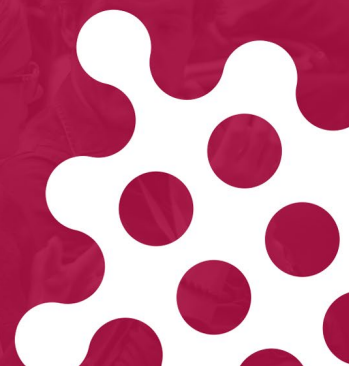




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**ABSTRACT**



**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 ( $C_{\text{trough}}$ ) 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  $\geq 1$  ICZ  $C_{\text{trough}}$ . ICZ started by day 9 post HCT. ICZ  $C_{\text{trough}}$  levels were checked when patients had been on a stable dose of oral ICZ for  $\geq 1$  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  $C_{\text{trough}}$  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  $\geq 2$  ICZ  $C_{\text{trough}}$  measured. A total of 109 ICZ  $C_{\text{trough}}$  were obtained at a median of 31 (interquartile range [IQR]: 23-41) days from HCT infusion. In LET group, ICZ  $C_{\text{trough}}$  were obtained after 16 (IQR: 2-22) days from LET initiation. The median  $C_{\text{trough}}$  was 3.0 (IQR: 2.2-4.2)  $\mu\text{g/mL}$  for all patients. ICZ  $C_{\text{trough}}$  were similar between no-LET and LET groups (**Figure 2**). Twenty patients with GI GVHD had 27 ICZ  $C_{\text{trough}}$ . ICZ  $C_{\text{trough}}$  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<sub>trough</sub> were within the expected range with or without LET coadministration in allogeneic HCT. Given reported decrease in C<sub>trough</sub> 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 (%)	
<b>Age</b>	Median (IQR), years	57 (51, 66)	58 (47, 64)	0.673
<b>Gender</b>	Male	50 (72)	11 (55)	0.139
<b>Underlying disease</b>	Leukemia/MDS	47 (68)	15 (75)	0.823
	Lymphoma	12 (17)	3 (15)	
	Other hematologic malignancy	10 (14)	2 (10)	
<b>Donor type</b>	Matched related/unrelated	45 (65)	9 (45)	0.260
	Mismatched related/unrelated	16 (23)	7 (35)	
	Haploidentical	8 (12)	4 (20)	
<b>HCT source</b>	Bone marrow	13 (19)	2 (10)	0.118
	Cord blood	8 (12)	6 (30)	
	Peripheral blood	48 (70)	12 (60)	
<b>Conditioning</b>	Myeloablative	37 (54)	10 (50)	0.775
	Reduced/ Non-myeloablative	32 (46)	10 (50)	
<b>GvHD prophylaxis</b>	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<sub>trough</sub>

