

Safety of Isavuconazole Compared with Voriconazole as Primary Antifungal Prophylaxis in Allogeneic Hematopoietic Cell Transplant Recipients

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Background

- Voriconazole (VCZ) antifungal prophylaxis (AFP) is frequently discontinued in allogeneic hematopoietic cell transplant recipients (allo-HCT) due to toxicities. We analyzed two matched cohorts of HCT patients from the same institution who received isavuconazole (ICZ) or VCZ AFP up to D100 post HCT.
- We report on: 1) rates of AFP premature discontinuation (d/c), 2) changes in transaminases values from start to end of treatment (EOT) and 3) rates of invasive fungal infections (IFI) and mortality by Day (D) +180 post HCT between VCZ and ICZ AFP.

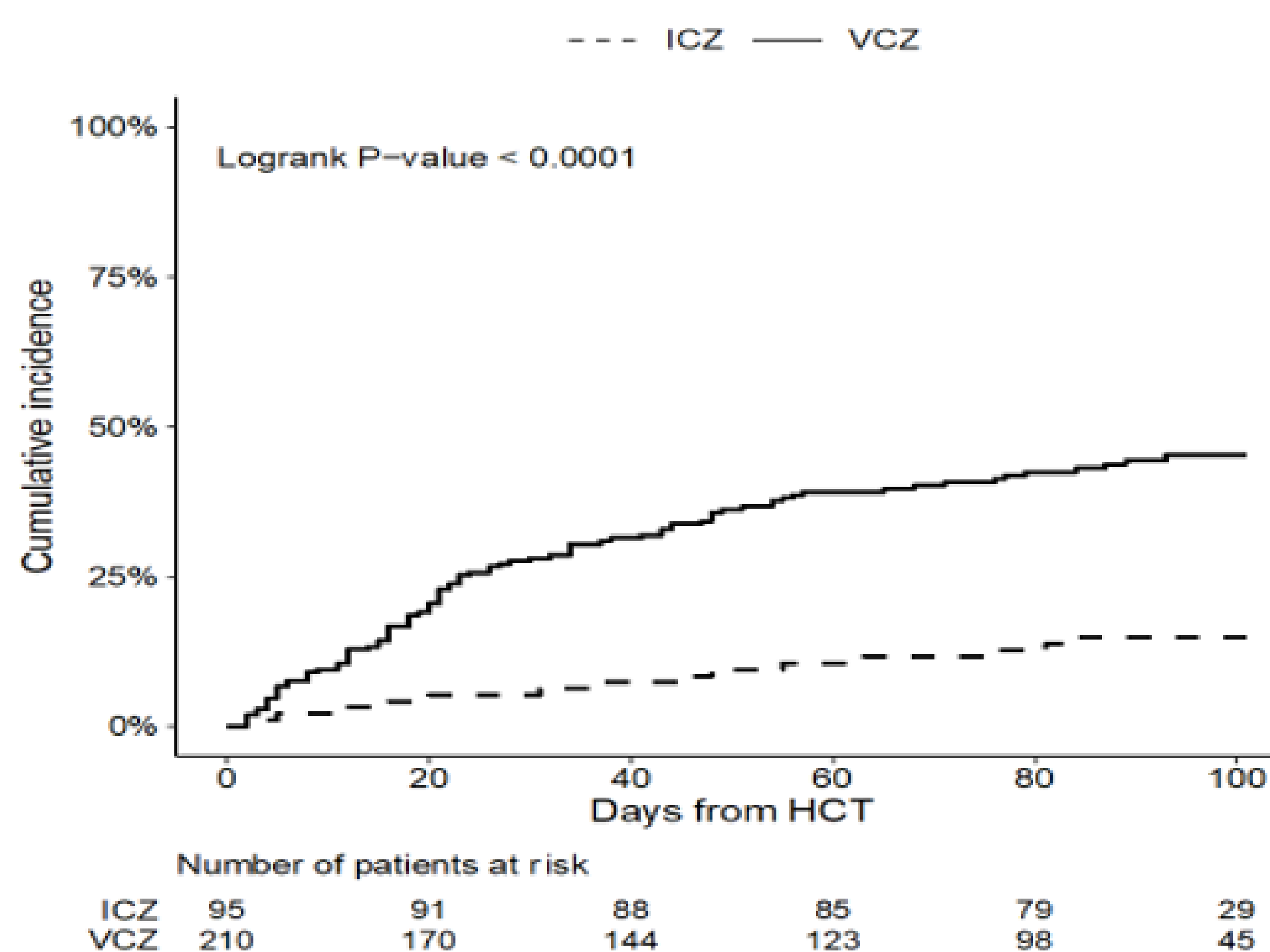
Methods

- Retrospective cohort study. Patients were matched by age, gender, underlying disease, conditioning regimen intensity, donor type, stem cell source and HCT-type using propensity score.
- Premature d/c of AFP was defined as d/c due to IFI or AE by D100 post HCT or interruption of >14 days for any reason.

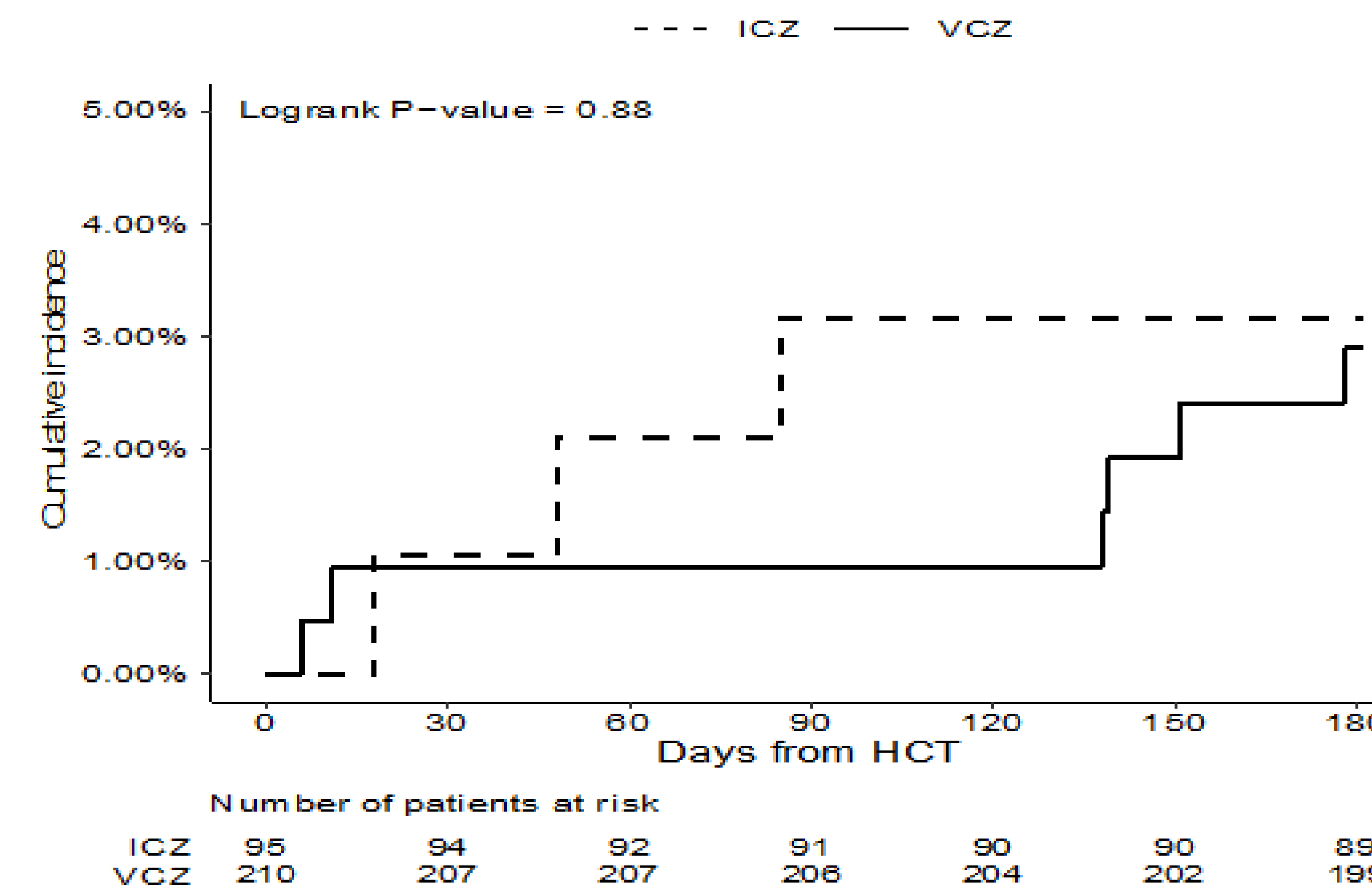
Results

Cohort	Number of patients	Setting	Time period
VCZ	210	Standard of care	9/1/2014-12/31/2015
ICZ	95	Open label clinical trial	7/1/2017-10/31/2018

VCZ was discontinued earlier and more frequently than ICZ



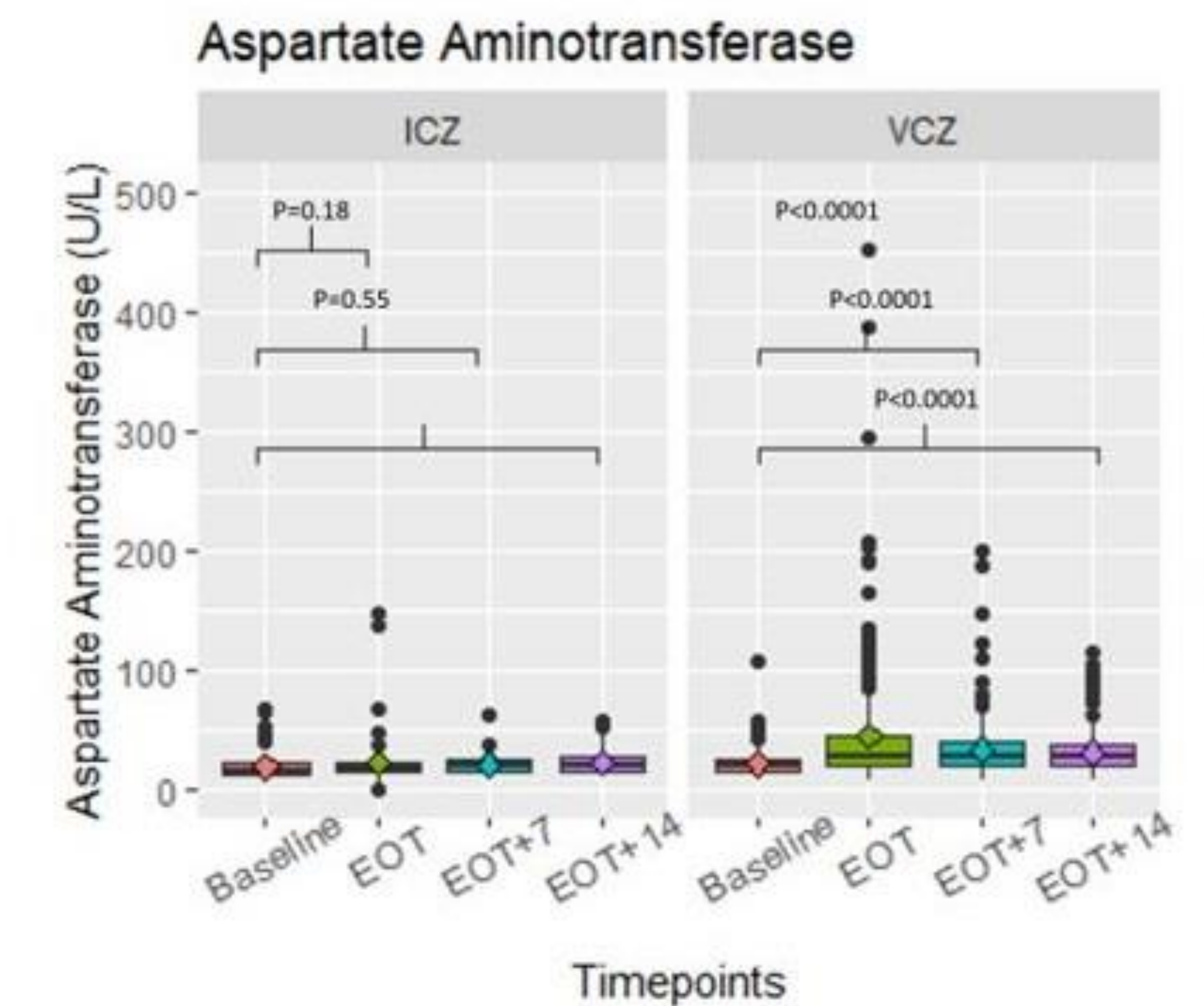
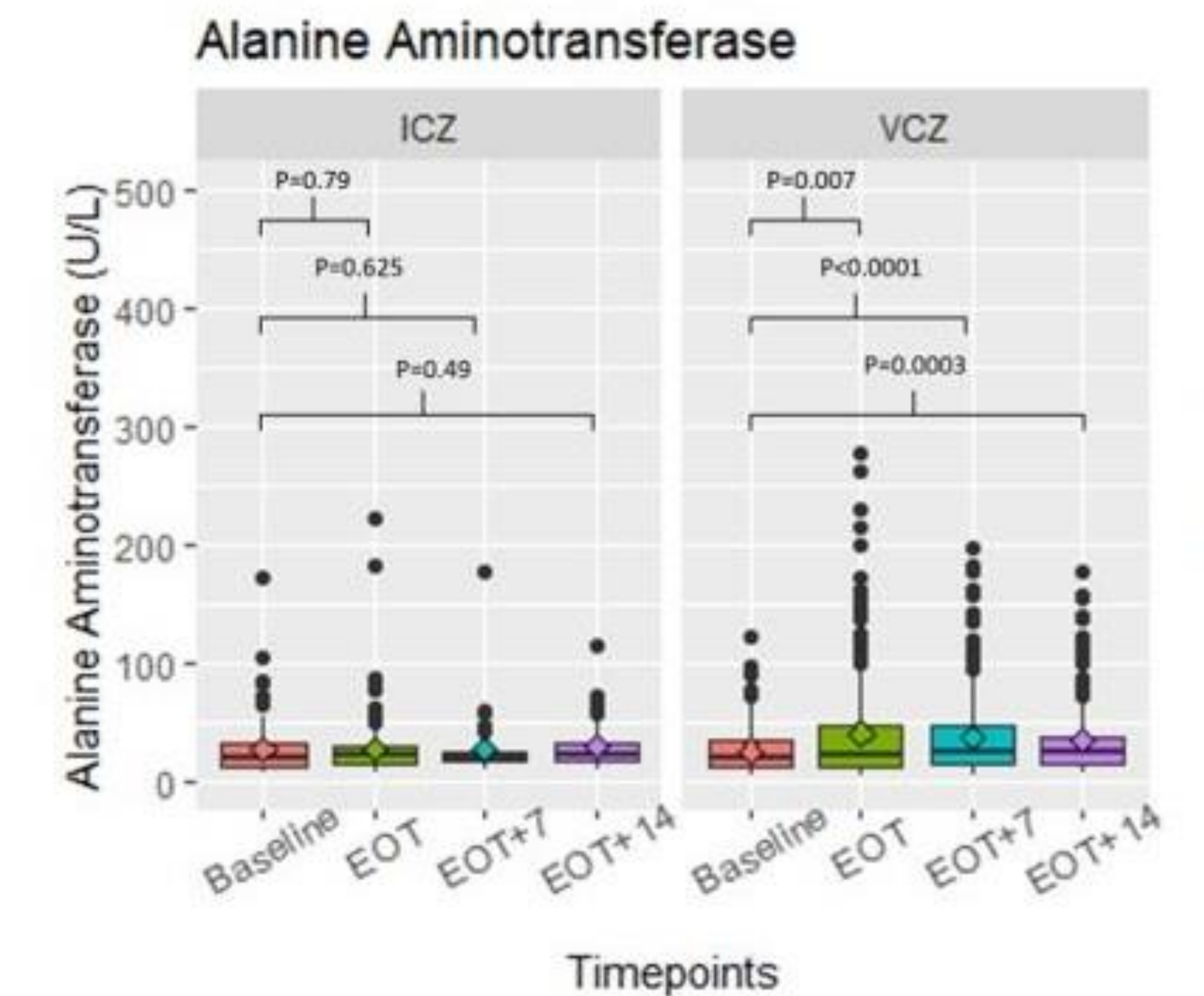
Similar incidence of IFI by D180 was similar between VCZ and ICZ cohorts



Breakthrough candidemia was more common in ICZ cohort

IFI Type	VCZ	ICZ
	Number of pts/ Days post HCT	Number of pts/ Days post HCT
<i>C. Parapsilosis</i>	0	2 D17, D47
<i>C. Glabrata</i>	1 D177	1 D84
Probable aspergillosis (based on GMA)	3 D5, D10, D138	0
Probable IFI (based on BDG)	2 D137, D150	0

Transaminases were elevated up to 2 weeks post EOT in VCZ but not ICZ cohort



- In ICZ cohort there was no change in transaminases compared to baseline.
- In VCZ cohort, ALT/AST remained elevated up to 14 D post EOT.

Conclusions

- In the first 3 months post HCT, isavuconazole AFP was better tolerated compared with voriconazole AFP.
- There was 66% less premature discontinuation with ICZ compared to VCZ and similar incidence of IFI by D180.
- Our data support the use of ICZ as a safer alternative to VCZ for primary antifungal prophylaxis in the first 3 months post HCT.

AFP	Duration days, median (IQR)	P-value	Premature discontinuation, %	P-value
VCZ	76 (23-94)		48.3	
ICZ	94 (87-100)	<0.0001	14.7	<0.0001