Initial treatment of cancer patients with fluconazole-intermediate *Candida glabrata* fungemia with an echinocandin or polyene is associated with better survival than initial treatment with an azole

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BACKGROUND

Candida glabrata is one of the three most frequent *Candida* species causing invasive candidiasis, and is the main species exhibiting multi-drug resistance (MDR).

In population and single-center studies, *C. glabrata* isolates are often non-susceptible to azoles, which should be used with caution against this pathogen[1].

A recent study[2] showed comparable outcomes between azoles and echinocandins for treatment of *C. glabrata* fungemia. There is paucity of data regarding clinical outcomes in cancer patients with *C. glabrata* fungemia treated with azoles, compared to those treated with other antifungals.

AIM

To compare all-cause mortality between cancer patients with *C. glabrata* fungemia treated within the first 48 hrs after blood culture collection with an azole and those treated with an echinocandin or polyene.

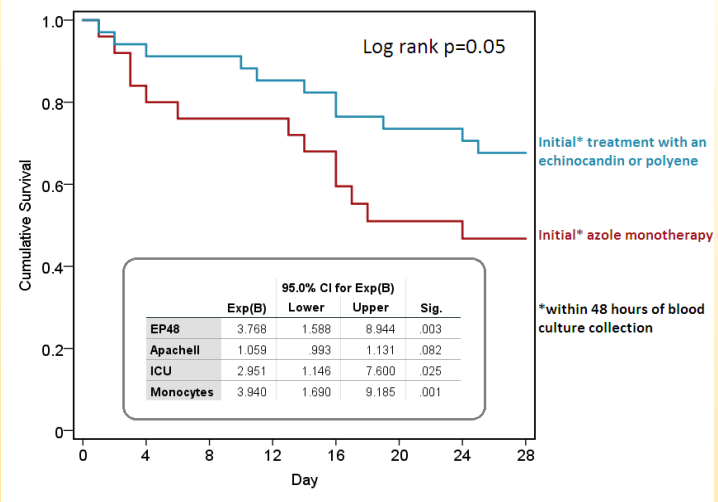

Figure 1: Kaplan-Meier curves and multivariate Cox regression analysis comparing 28-day all-cause mortality between cancer patients with *C. glabrata* fungemia treated within the first 48 hours after blood culture collection with azole monotherapy and an echinocandin or polyene.

Table 1: Baseline Parameters (n (%) or mean ± SD)

Parameter	Azole monotherapy	Echinocandin/polyene	P
Gender (F)	11 (44)	22 (51)	0.6
Age (years)	57 ± 14	54 ± 15	0.4
Acute leukemia	3 (12)	7 (16)	0.6
HSCT	4 (16)	2 (5)	0.1
ANC <500/μL	4 (16)	10 (23)	0.5
ALC <100/μL	4 (16)	13 (30)	0.2
AMC <100/μL	7 (28)	14 (33)	0.7
ICU	7 (28)	23 (54)	**0.04**
APACHE II score	14 ± 7	15 ± 6	0.4
Central line-related candidemia	12 (48)	23 (54)	0.7
Diabetes	4 (16)	6 (14)	0.8
CKD	6 (24)	7 (16)	0.4
AKI	6 (24)	21 (49)	**0.04**
28-day mortality	13 (52)	13 (30)	**0.07**

HSCT: Hematopoetic Stem Cell Transplantation; ANC, ALC, AMC: Absolute Neutrophil, Lymphocyte, Monocyte Counts; CKD: Chronic Kidney Disease; AKI: Acute Kidney Injury; ns: non-significant (p>0.1)

RESULTS

- 68 patients were studied. 33 (49%) were female and the mean age (SD) was 55 (15) years.
- 10 patients (16%) had acute leukemia.
- 14 patients (21%) were neutropenic (absolute neutrophil count <500 neutrophils/μL).
- 28-day survival was 70% (30/43) with initial echinocandin or polyene, and 48% (12/25) with initial azole monotherapy (p=0.07) (Table 1).
- 28-day survival in neutropenic patients was 50% (5/10) with initial echinocandin or polyene and 25% (1/4) with initial azole treatment.
- In multivariate Cox regression analysis, ICU stay (HR 3, p = 0.025), APACHE II score (HR 1.1, p=0.08), monocytopenia (<100/μL, HR 4, p=0.001), and azole monotherapy within the first 48 hrs after blood culture collection (HR 2.2, p=0.003) were associated with increased 28-day mortality (Fig. 1).

METHODS

Retrospective review of clinical and laboratory data of cancer patients with ≥1 blood culture positive for fluconazole-intermediate (MIC ≤ 32 mg/L) *C.glabrata* at MD Anderson Cancer Center (3/05 – 9/13), all of whom received antifungal treatment within the first 48 hrs after blood culture collection.

CONCLUSIONS

In this small series of cancer patients with *C. glabrata* fungemia, excluding those who did not receive an antifungal or had fluconazole-resistant isolates, there was a trend towards increased all-cause mortality with azole monotherapy, after adjustment for other clinical confounders.

These findings support the IDSA recommendation[3] for use of echinocandins as first line treatment in *C. glabrata* candidemia.

An azole as initial treatment should be avoided in cancer patients with suspected *C. glabrata* fungemia, including those without neutropenia.

References: [1]Farmakiotis et al, Clin Microbiol Infect 2015;21(1):79, [2]Puig-Asensio et al, Antimicrob Agents Chemother 2016;60(6):3291, [3]Pappas et al, Clin Infect Dis 2016;62(4):409.