

DETERMINING OPTIMAL ANTIFUNGAL PROPHYLAXIS IN ACUTE MYELOID LEUKEMIA PATIENTS RECEIVING VENETOCLAX



THE UNIVERSITY OF KANSAS HEALTH SYSTEM

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BACKGROUND

- Venetoclax in combination with a hypomethylating agent (HMA) was recently approved in 2018 by the FDA for the treatment of acute myeloid leukemia (AML) in elderly patients¹
- Previous studies have shown better outcomes in patients taking venetoclax in combination with hypomethylating agents (azacitadine and decitabine) compared to HMA monotherapy²
- Patients who receive venetoclax with HMA often have prolonged periods of pancytopenia, specifically neutropenia and thrombocytopenia¹
- Because of prolonged neutropenia, studies recommend antifungal prophylaxis to prevent invasive fungal infections (IFIs), but no specific agents have been recommended¹
- At The University of Kansas Healthcare System (TUKHS), the preferred antifungal agent has not been established
- Azole antifungals inhibit CYP3A4 (either moderately or strongly) which metabolizes venetoclax; this drug interaction prompts empiric dose reductions of venetoclax and may lead to increased cytopenias with venetoclax³

STUDY OBJECTIVES

- Primary Objective:** Determine the rate of IFI in patients prescribed fluconazole, posaconazole, other antifungal, or no antifungal prophylaxis
- Secondary Objectives:** Determine the duration of neutropenia and thrombocytopenia

STUDY DESIGN and METHODS

- Single-center, retrospective cohort study evaluating patients treated at TUKHS from November 2018 through January 2020
 - Included patients at least 18 years old and those who received venetoclax with HMA for AML or myelodysplastic syndrome (MDS)
 - Excluded patients who received less than one month of therapy or those who were lost to follow-up within 3 months
- Statistical analysis via chi square test (SPSS Version 27)

RESULTS

Baseline Characteristic	N=96	Baseline Characteristic	N=96
Age (median, range)	67 years (18-89)	TP53 Mutation (%)	
Sex (%)		Present	30 (31)
Male	54 (56)	Not present	65 (68)
Female	42 (44)	AML Subtype (%)	
Diagnosis (%)		De novo	53 (56)
AML	95 (99)	Therapy Related	3 (3)
MDS	1 (1)	Secondary	39 (41)
		AML Setting (%)	
		Newly Diagnosed	60 (63)
		Relapsed/Refractory	36 (37)

RESULTS

Patients				
Treatment Characteristic	N=96	Drug		P-value
		Yes	No	
Venetoclax Dosing (%)				
50 mg	1 (1)			
100 mg	38 (40)			
200 mg	43 (45)			
400 mg	4 (4)			
Hypomethylating Agent (%)				
Azacitadine	51 (53)			
Decitabine	45 (47)			
5-day induction	17			
10-day induction	28			
Antifungal Agent (%)*				
Posaconazole	46 (48)			
Fluconazole	32 (33)			
Isavuconazole	9 (9)			
Voriconazole	5 (5)			
None	5 (5)			
Micafungin	1 (1)			

*24 Patients' antifungal agents were switched

Figure 1: IFI by Antifungal

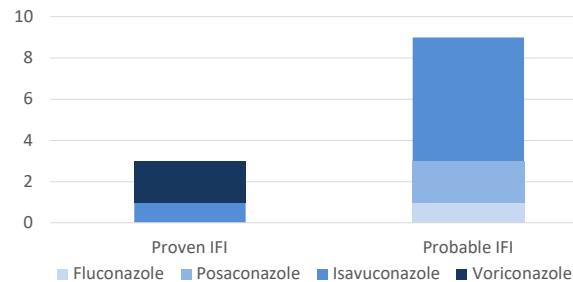
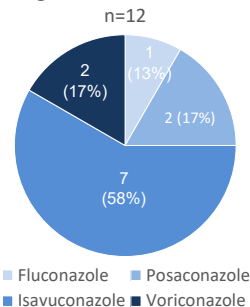
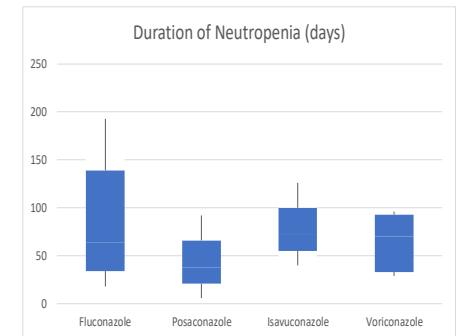


Figure 2: Incidence of IFI n=12



RESULTS

- Figure 3: Duration in days of Neutropenia by Antifungal



DISCUSSION

- No difference in IFIs when comparing fluconazole with posaconazole (p=1.0)
- When comparing posaconazole and fluconazole to other antifungals used, posaconazole and fluconazole had significantly less IFIs (p=0.001)
- Posaconazole had a clinically significant shorter duration of both neutropenia and thrombocytopenia
- Posaconazole may be preferred due to extended coverage of aspergillus infections that fluconazole lacks
- Limitations include:
 - Retrospective, single-center study
 - Low rate of fungal infections makes for a small patient size

CONCLUSIONS

- All patients who developed fungal infections had prolonged neutropenia
- Rates of IFI are too similar for fluconazole versus posaconazole to determine if one is more beneficial
- Observed increase in IFIs for isavuconazole
- Recommend avoiding isavuconazole for antifungal prophylaxis

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CONTACT INFORMATION

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Disclosures: All authors of this presentation have nothing to disclose.