Incidence of Invasive Fungal Infections in Previously Untreated Patients with Acute Myeloid Leukemia Receiving Venetoclax and Azacitidine

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Background

- Acute myeloid leukemia (AML) is associated with a poor prognosis, particularly in elderly patients with comorbidities
- Combined azacitidine (AZA) with the BCL-2 inhibitor venetoclax (VEN) improved outcomes compared to AZA alone
- Primary Objective: determine if antifungal prophylaxis is beneficial for AML patients treated with VEN/AZA
- Primary Outcome: incidence of IFI during VEN/AZA therapy
- Secondary Outcomes: impact of patient demographics, duration of neutropenia, AML-specific risk factors, and receipt of antifungal prophylaxis

Methods

- Study Type: retrospective cohort study conducted at the University of Colorado Hospital (UCH)
- Patient Criteria: Patients with newly diagnosed AML treated at UCH between January 2014 and August 2020 with VEN/AZA
- Duration of VEN/AZA Therapy: time from initiation of induction therapy until: 1) patient discontinuation, 2) progression of disease, 3) bone marrow transplantation, 4) death
- IFI Classification: “proven”, “probable”, “possible” (based on EORTC/MSGERC definition)
- Statistics: Multivariable analysis using binary logistic regression

Patient Classifications

Characteristic	Results (n=144)
Age (years), median (IQR)	72 (66, 76)
Sex, female	71 (49)
AML Classification	
Secondary AML	56 (39)
De novo AML	44 (31%)
ELN Classification	
Unknown/unable to assess	5 (3.5)
Unfavorable	92 (64)
Intermediate	23 (16)
Favorable	24 (17)
VEN/AZA Duration (days), median (IQR)	137 (56, 268)
Duration of Neutropenia (days), median (IQR)	35 (19, 58)
Antifungal Prophylaxis*	10 (6.9)
Anidulafungin	6 (60)
Azole	5 (50)
Fluconazole	4 (80)
Isavuconazole	1 (20)
Antifungal prophylaxis duration (days), median (IQR)	31 (12, 58)

Table 1: Demographics and Classification of AML Patients. IQR = Interquartile Range; ELN = European LeukemiaNet. Results are presented as number of patients (n) followed by percentages in parentheses, unless otherwise specified. *May have received one more than antifungal agent

Patient Categorization

Variable	IFI (n=25)	No IFI (n=119)	P-Value
Neutropenia ≥30 days	20 (80)	61 (51)	0.01
Age ≥65 years	15 (60)	58 (49)	0.31
Sex, Female	10 (40)	61 (51)	0.04
Unfavorable ELN Classification	13 (52)	55 (46)	0.60
Antifungal Prophylaxis	0 (0)	10 (8.4)	0.21
	Proven/Probable IFI (n=8)	No Proven/Probable IFI (n=136)	
Neutropenia ≥30 days	7 (88)	74 (62)	0.07

Table 2: Patients categorized based on Neutropenia, Age, Sex, ELN classification, and antifungal prophylaxis versus incidence or no incidence of IFI.

Results

- 144 VEN/AZA-treated AML patients
- 25 (17%) total cases of IFI
- 8 (5.6%) cases classified as “proven” or “probable”
- Sites of Infection: pulmonary only
  - no cases of sino-nasal, CNS, GI, or fungaemic sites of suspected IFI
- 10 (6.9%) patients received antifungal prophylaxis with VEN/AZA therapy
  - no cases of IFI reported

Discussion

- Rate of proven and probable IFI: 5.6% (consistent with existing literature; lower than alternative AML treatment regimens)
- Multivariable regression associated incidence of IFI with duration of neutropenia ≥ 30 days (Odds Ratio [OR]= 0.27, 95% Confidence Interval [CI]=0.10-0.78, P=0.01)
- No significant association between IFI and age, sex, ELN classification, or antifungal prophylaxis
- Limitation: small sample size
  - not adequately powered to conclude if antifungal prophylaxis significantly impacted incidence of IFI
- Proposed Recommendation: Local rates of IFI should influence decision between universal antifungal prophylaxis protocol versus a pre-emptive monitoring protocol
  - protocol should vary depending between each institution

No Disclosures