Breakthrough Invasive Pulmonary Aspergillosis During Isavuconazole Prophylaxis in Patients with Hematologic Malignancies: A single Center Experience

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Background

- Prophylaxis against invasive mould fungal infection (IMI) is recommended in those with high-risk hematologic malignancies and hematopoietic cell transplant (HCT) recipients
- Isavuconazole (ISA) is an attractive candidate for prophylaxis due to its broad spectrum activity, ease of dosing, favorable side effect profile, and limited drug-drug interactions
- However, clinical experience with the use of ISA as prophylaxis is lacking

Research Objectives

- Primary Objectives:
  - Describe institutional clinical experience using ISA as a first-line prophylactic agent over a 13 month period (9/1/2016 to 9/31/2017)
  - Characterize breakthrough IMIs during receipt of ISA prophylaxis
  - Compare incidence of IMIs during ISA prophylaxis to other mould-active agents at our center

Methods (Cont.)

- Exclusion Criteria:
  - Previous IMI requiring secondary prophylaxis or receiving ISA for treatment of established infection
  - < 7 days of primary prophylaxis

Methods

METHODS

Design:

- Retrospective cohorts of high risk inpatients and outpatients with hematologic malignancy and/or hematopoietic cell transplant (HCT) at Oregon Health and Science University

IFI primary prophylaxis indicated in the following:

- New AML, refractory/relapsed AML, MDS
- Post-allogeneic HCT:
  - Primary prophylaxis if ≥ 14 days neutropenia prior to HCT
  - Graft versus host disease (GVHD) or other conditions requiring high dose steroids

Inclusion Criteria:

- Patient population:
  - AML undergoing induction, re-induction, or salvage chemotherapy
  - MDS undergoing chemotherapy
  - Post-allogeneic HCT meeting criteria above
  - ≥ 7 days uninterrupted ISA primary prophylaxis

Outcomes:

- Primary Outcomes:
  - Breakthrough probable or proven IMI per EORTC/MSG criteria
  - If uncertainty about a diagnosis the case underwent independent, blinded review by 2 transplant ID clinicians
- Secondary Outcomes:
  - Duration of neutropenia and duration of prophylaxis prior to IFI
  - Understand characteristics about predisposing factors that could lead to IFI

Results

Table 1: Characteristics of patients on ISA prophylaxis

Table 2: Indications for ISA prophylaxis per course

Table 3: Characteristics of IFI breakthrough infections while on ISA prophylaxis

Table 4: Breakthrough rate per antifungal course and indication (2015 to the present)

Discussion

- Incidence of breakthrough probable or proven IPA on ISA was greater than expected despite adequate ISA serum levels
- Due to unexpected high rate of IPA on ISA our institution switched back to POS for primary prophylaxis
- After switching back to POS there have not been any breakthrough infections

Strength:

- All patients were high risk for IFI warranting prophylaxis

Limitation:

- Single center retrospective study which limits the generalizability of results

Future endeavors:

- Analyze for breakthrough IFI from 2017 to 2018 with POS and VOR as our formulary medications for primary prophylaxis

Conclusion:

- Further studies are needed to determine the role of ISA prophylaxis in high risk hematologic malignancy patients

References