Antifungal Prophylaxis in APL: The Azole Dilemma During ATO Induction

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Background:

- NCCN guidelines specify the use of posaconazole for prolonged neutropenia in acute leukemias
- The use of azoles with arsenic trioxide (ATO) is limited by drug-drug interactions that can result in hepatotoxicity and QTc prolongation requiring interruptions to cancer-directed therapy.
- This study evaluated the risk of fungal infections with contemporary APL regimens and investigated outcomes using various antifungal prophylaxis strategies.

Methods:

- Retrospective evaluation of APL patients treated at Mount Sinai from 2012 – 2026.
- 70 patients were included in this review.

Results:

•Median (IQR) duration of neutropenia was 14 days (9 - 18) and median duration of antifungal prophylaxis was 17 days (10 - 27).

Antifungal Agent	N = 70
Posaconazole	21
Voriconazole	8
Isavuconazole	5
Fluconazole	3
Caspofungin	18
Micafungin	1
No Fungal Prophylaxis	14

Table 1: Number of patients per antifungal agent.

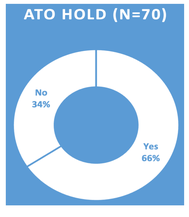

Figure 2: Percentage of patients that required an ATO hold during induction therapy.

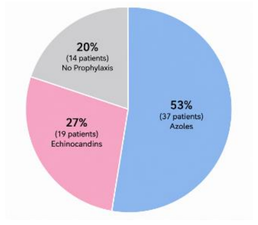

Figure 1: Percentage of patients by antifungal class.

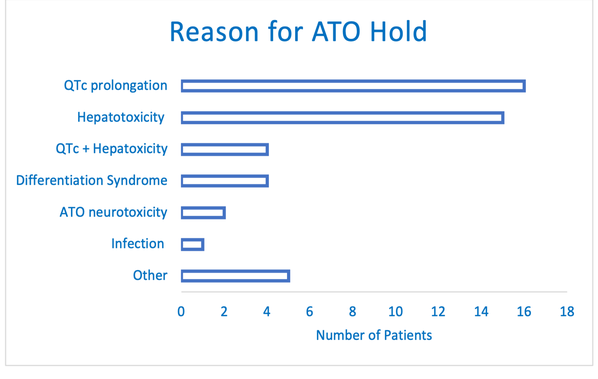

Figure 3: Distribution of patients by reason for ATO hold. "Other" represents additional combinations of listed side effects.

- Prophylaxis was switched for 26 patients (46%)
- 15 (58%) switched from an azole to echinocandin due to:
  - hepatotoxicity (53%)
  - QTc prolongation (27%)
  - provider preference (20%)

Patients who had their prophylaxis switched from an azole to echinocandin had a median 4 (2 - 12) days of ATO dose interruption compared to a median of 23 (9 - 33) days of ATO dose interruption for those switched from an azole to another azole (p = 0.08).

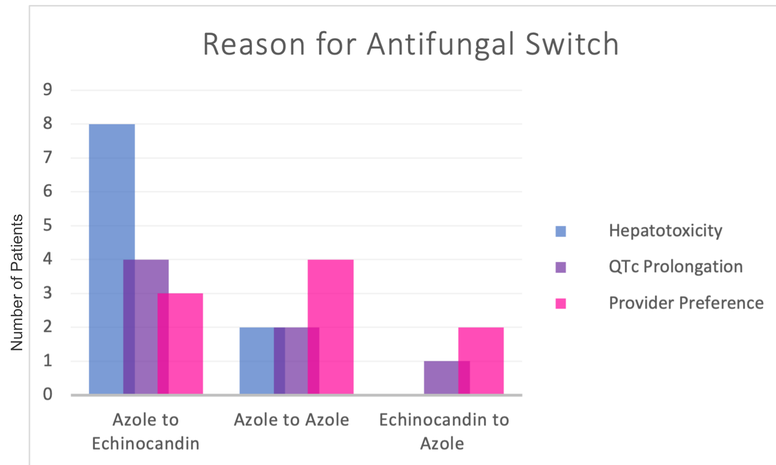

Figure 5: Antifungal class switch by side effect profile.

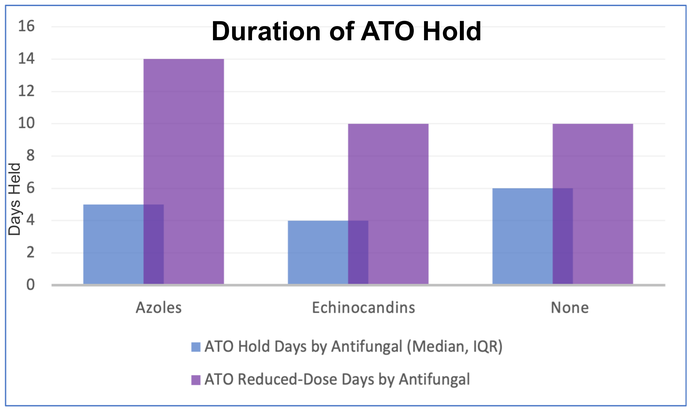

Figure 4: Number of days ATO was held/dose reduced per antifungal class.

Documented Fungal Infections:

- 5 (7%) patients developed fungal infections
  - 2 patients developed thrush
  - 1 patient developed a superficial fungal rash
  - 2 patients developed possible pulmonary invasive fungal infections (IFI)
- 4 (80%) were not on prophylaxis at the time of infection
  - 1 IFI breakthrough occurred on caspofungin (20%), though Infectious Diseases had low suspicion for true IFI.

Conclusion:

- Fungal infections in APL are rare regardless of prophylaxis strategy.
- Echinocandins may offer equivalent prophylaxis to azoles while resulting in fewer ATO dose modifications for hepatotoxicity and QTc prolongation.
- Our analysis did not reach statistical significance, highlighting the importance of studying prophylaxis strategies in larger cohorts.