Abstract #AML-1452

Invasive Fungal Infections in Acute Myeloid Leukemia: Emerging Challenges in the Era of Targeted Therapy and Cellular Immunotherapy

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1 Introduction

- Invasive fungal infections (IFI) remain a major cause of morbidity and mortality in AML, particularly during intensive chemotherapy, prolonged neutropenia, and stem cell transplantation.
- Targeted and cellular therapies have altered infection risk and antifungal management.

2 Aim

- To review contemporary evidence on the evolving epidemiology, risk factors, and management challenges associated with invasive fungal infections in acute myeloid leukemia.

3 Method

- A structured literature review (2000-2025) was conducted using PubMed, Embase, and Scopus. Studies assessing epidemiology, fungal pathogens, antifungal prophylaxis, targeted therapies, breakthrough infections, and management strategies were reviewed.

5 Conclusions

- Invasive fungal infections remain a major challenge in AML despite advances in antifungal prophylaxis and supportive care.
- Optimized, risk-adapted prophylaxis with early diagnostic-driven treatment remains critical to reducing IFI-related morbidity and mortality.

4 Results

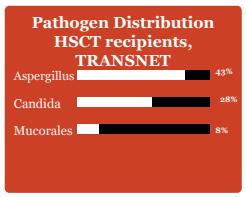
- Invasive aspergillosis remains the predominant fungal infection across contemporary AML cohorts.
- Novel targeted therapies (venetoclax, FLT3 inhibitors) have increased prophylaxis complexity through significant azole drug interactions.
- Non-Aspergillus molds, including Mucorales, are increasingly detected in heavily pretreated and transplant populations.
- Contemporary management emphasizes early imaging, biomarker surveillance, and risk-adapted antifungal stewardship.

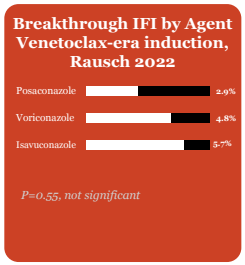
DOES TARGETED PROPHYLAXIS REDUCE IFI AND MORTALITY?

Cornely et al. 2007 (NEJM RCT, N=602) — posaconazole vs. standard prophylaxis in high-risk AML/MDS induction

IFI Incidence	IFI-Attributable Mortality
8% → 2%	**9% → 5%**
standard → posaconazole	standard → posaconazole

P<0.001 for both outcomes — directly answers this review's primary question





Also rising: non-Aspergillus molds (incl. Mucorales), especially in heavily pretreated patients and transplant recipients.

Representative Evidence Base

Study	Design (N)	Key Finding
Cornely et al. 2007 (NEJM)	RCT, N=602	Posaconazole vs fluconazole/itraconazole in AML induction: proven/probable IFI 2% vs 8% (P<0.001); improved overall survival.
Kontoyiannis et al. 2010 — TRANSNET	Prospective surveillance, N=16,200	HSCT recipients: 12-month cumulative IFI 3.4-8.1%; Aspergillus most frequent (43%), 1-year survival with IA ~25%.
Cornely et al. 2021	Prospective Phase II, N=65	Isavuconazole prophylaxis: breakthrough IFI 3-6%; no QTc prolongation, reduced drug interactions vs posaconazole.
Rausch et al. 2022	Retrospective cohort, N=277	Venetoclax-era induction: breakthrough IFI 2.9-5.7% across mold-active triazoles, no significant difference.

Mechanism: Why Targeted Therapy Complicates Antifungal Prophylaxis

Azole Prophylaxis
Posaconazole / Voriconazole / Isavuconazole

↓

Inhibits CYP3A4
Hepatic drug-metabolizing enzyme

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↑ Drug Levels
Venetoclax, Midostaurin, Gilteritinib accumulate

↓

Dose Adjustment Required
Typically 50-75% dose reduction needed

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