

# ADVANCES IN LLM

Current Developments in the Management of Leukemia, Lymphoma, and Myeloma

Section Editor: Susan O'Brien, MD

## Preventive Strategies for Invasive *Aspergillus* in Acute Myelogenous Leukemia



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### **H&O** What are the causes of fungal infection in patients with acute myelogenous leukemia (AML)?

**GS** Fungal infections are infrequent but not rare in the setting of AML. Outside the environment of hematopoietic stem cell transplant, prolonged neutropenia and the use of broad-spectrum antibacterial antibiotics contribute to the selection for fungal infection. In the transplant setting, an additional proximate cause is the use of corticosteroids for prevention and/or management of graft-vs-host disease.

### **H&O** What is the potential impact of a fungal infection in a patient with AML?

**GS** Fungal infections are potentially life-threatening. Patients with AML usually develop hyphal fungal infections with *Aspergillus* and similar organisms that are difficult to manage. Invasive *Aspergillus* has the greatest risk of an unfavorable outcome. It is associated with prolonged neutropenia and extended exposure to antibacterial antibiotics. *Mucor* is less common, but is also associated with prolonged neutropenia and/or neutrophil dysfunction. Patients with AML can also develop pseudohyphal infection with *Candida*, which is easier to treat than *Aspergillus*.

### **H&O** What are the risk factors for developing a fungal infection in AML?

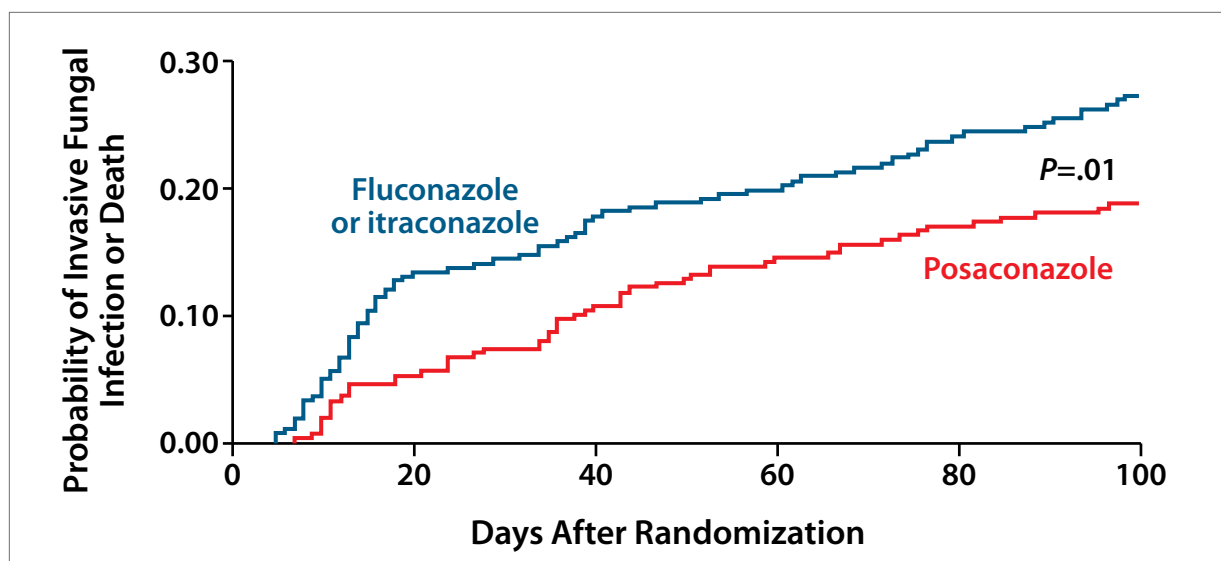
**GS** Prolonged neutropenia and the use of broad-spec-

trum antibacterial antibiotics put a patient at high risk for infection. When febrile neutropenia persists despite the use of broad-spectrum parenteral antibacterial antibiotic therapy, the standard of care is to administer an antifungal agent as empiric therapy.

### **H&O** What types of antifungal agents are used as empiric therapy?

**GS** The azoles are particularly effective. At my institution, we have switched almost entirely to posaconazole (Noxafil, Merck) as our empiric antifungal agent of choice because of its generally good coverage of *Aspergillus*. In a randomized trial comparing posaconazole vs fluconazole or itraconazole for the prevention of invasive fungal infections among patients with neutropenia who were undergoing remission-induction chemotherapy for AML or myelodysplastic syndrome, posaconazole was associated with significantly fewer cases of invasive aspergillosis and significantly longer survival (see the figure). The echinocandins also have some activity, but their inhibitory concentrations are inferior to those achieved with the new azole drugs for hyphal fungal infections. Liposomal amphotericin and isavuconazonium sulfate (Cresemba, Astellas) are used in the management of mucormycosis.

Granulocyte transfusions have activity as well. They play an important role in patients with disease that is unresponsive to the current antifungals.



**Figure 1.** Time to invasive fungal infection or death among patients receiving posaconazole vs fluconazole or itraconazole for the prevention of invasive fungal infection in a randomized trial. Adapted from Cornely OA et al. *N Engl J Med.* 2007;356(4):348-359.

### H&O Are there other preventive strategies for invasive *Aspergillus* in AML?

**GS** The aim is to decrease patients' exposure to invasive *Aspergillus*. It is important for patients to stay in rooms that have not undergone recent construction and are filtered by high-efficiency particulate arrestance (HEPA). There might be a role for more intensive reverse isolation, but that approach is no longer used as frequently. Prophylactic antifungal agents are often used in the setting of hematopoietic stem cell transplantation.

### H&O How is the diagnosis of a fungal infection in AML confirmed?

**GS** Invasive *Aspergillus* is the most difficult fungal infection to confirm. Diagnostic imaging can provide suggestive, supportive, and circumstantial evidence of fungal infection. A fungal infection can be indicated by plain radiography or computed tomography scans showing pulmonary lesions that are not otherwise attributable to a bacterial infection. Although culture or

histologic confirmation are the gold standards for diagnosis, they are difficult to obtain. Typically, a culture of bronchoalveolar lavage fluid is obtained in a patient with a lung infection. Culture of blood or urine will not identify a fungal infection, even in a patient with a high clinical likelihood.

#### Disclosures

*Dr Schiller has no real or apparent conflicts of interest to report.*

#### Suggested Readings

Cornely OA, Maertens J, Winston DJ, et al. Posaconazole vs. fluconazole or itraconazole prophylaxis in patients with neutropenia. *N Engl J Med.* 2007;356(4):348-359.

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