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Micafungin
A Viewpoint by Dimitrios P. Kontoyiannis

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Micafungin is a large cyclic lipopeptide and belongs to a new class of antifungals, the echinocandins. Echinocandins have a unique mechanism of action by inhibiting β-(1,3)-D-glucan synthase, a fungus-specific target involved in cell wall biosynthesis. Micafungin shows rapid fungicidal activity *in vitro* against a variety of *Candida* spp., including non-albicans and azole-resistant *Candida* spp., even though the minimum inhibitory concentration of some *Candida* spp. (e.g. *C. parapsilosis*) is high. However, the clinical relevance of the *in vitro* susceptibility of *Candida* spp. to the echinocandins is not known. Nevertheless, micafungin has shown convincing activity in animal models of invasive candidiasis. The drug is inherently inactive against *Cryptococcus neoformans* and it has limited efficacy against *Pneumocystis jiroveci* (previously known as *P. carinii*) and the dimorphic fungii. The *in vitro* activity of micafungin against *Aspergillus fumigatus* is less impressive, since the echinocandins exert a complex pattern of inhibition against this fungus that results in death of only the actively growing hyphal tips. However, micafungin's activity in animal models of aspergillosis is quite good and comparable to that of amphotericin B. Finally, micafungin is not active against non-*Aspergillus* molds (e.g. *Fusarium* spp., *Zygomycetes* spp.).

This drug, like all of the echinocandins, is nonabsorbable, has predictable linear pharmacokinetics, minimal drug-drug interactions and its tolerability is excellent, even at high dosages. Its central nervous system penetration is not well studied, but it is probably limited.

The clinical data for the treatment of bloodstream candidiasis and aspergillosis with micafungin come from open-label studies and suggest a clinical role for this drug in the treatment of mycoses. In an era of concerns of azole resistance among *Candida* spp., it is believed that the echinocandins such as micafungin will play an important role in the treatment of candidiasis, especially in patients with severe comorbities (e.g. renal dysfunction, intensive care unit setting). For aspergillosis, the drug has been mainly used in combination with other licensed antifungals (especially amphotericin B or its lipid formulations) for refractory infections. A recent large, randomised, prophylaxis study comparing micafungin with fluconazole in neutropenic bone marrow transplantation recipients showed that micafungin was non-toxic and more effective than fluconazole in preventing invasive fungal infections, especially aspergillosis. Finally, micafungin was shown to be effective in the treatment of oesophageal candidiasis, even though its therapeutic role for this infection will probably be limited, in view of the lack of an oral formulation.

Micafungin has not been extensively studied in the paediatric population. Its relative efficacy in comparison to the other echinocandins (e.g. caspofungin, anidulafungin) and the newer generation triazoles (e.g. voriconazole) is not known. Pricing, safety profile and more clinical experience will probably influence the ultimate place of this very promising new antifungal among the other members of its class. ▲