JOURNAL OF CLINICAL MICROBIOLOGY, Feb. 2003, p. 911 Vol. 41, No. 2
0095-1137/03/$08.00+0 DOI: 10.1128/JCM.41.2.911.2003


# Letters to the Editor

## Multidrug-Resistant *Trichosporon asahii* Isolates Are Susceptible to Voriconazole

We recently described the recovery of six clinical isolates of *Trichosporon asahii* from nongranulocytopenic patients that exhibited reduced susceptibilities to amphotericin B, flucytosine, ketoconazole, itraconazole, and fluconazole (7). In a recent paper Paphitou et al. reported (6) that the new investigational triazoles including voriconazole were highly potent against 24 isolates of *Trichosporon asahii* (MIC and minimal fungicidal concentration [MFC] of 0.25 and 0.5 mg/liter, respectively), confirming the prior observation that voriconazole has a lower MIC for *T. asahii* than do other azoles (4).

Recently, the NCCLS has recommended testing yeasts for susceptibility to new triazoles including voriconazole (M27-A2) (5), and a commercial Etest kit for voriconazole has become available. Consequently, we performed susceptibility testing for our *T. asahii* multidrug-resistant isolates against voriconazole (7). The results (Table 1) strongly indicate that these six isolates, which exhibit reduced susceptibilities to fluconazole, are highly susceptible to voriconazole. The MICs and MFCs of voriconazole for these isolates are close (0.125 to 0.25 and 0.25 to 1.0 mg/liter, respectively), suggesting fungicidal activity of voriconazole.

Voriconazole is an expanded-spectrum synthetic triazole derivative of fluconazole. It inhibits the enzyme lanosterol 14-α-demethylase of *Candida albicans* and *Aspergillus fumigatus* with potencies 1.6 and 160 times greater, respectively, than those of fluconazole (3). Its potent fungicidal activity is likely due to the high affinity of voriconazole for fungal 14-α-demethylase, a concept supported by ultrastructural and biochemical analysis (1). However, unlike fluconazole, voriconazole also inhibits 24-methylene dihydrolanosterol demethylation of certain yeasts and filamentous fungi (3). These two reasons may explain why voriconazole may be effective in the treatment of mycoses like trichosporonosis that do not respond to other azoles. According to a new study, voriconazole is "superior" to amphotericin B for treating life-threatening invasive aspergillosis (2) and was recently approved in some European countries for the treatment of invasive aspergillosis.

In our previous paper (7) we emphasized the importance of the patient's basic immune status in determining the outcome of *T. asahii* infection. We concluded that in vitro resistance to antifungal drugs might not be critical in immunocompetent patients. However, immunocompromised patients may be dependent on fungicidal drug activity, so that infection with multidrug-resistant *T. asahii* isolates may be fatal in this population. Our new data with the low MICs and MFCs of voriconazole that confirm other in vitro studies suggest that voriconazole may offer a clinical solution in trichosporonosis when other antifungal drugs fail.

TABLE 1. Susceptibilities of *T. asahii* isolates to fluconazole and voriconazole

| Patient no. (isolate no.) | MIC[a] (mg/liter) | | MFC[b] (mg/liter) | |
|---|---|---|---|---|
| | Fluconazole | Voriconazole | Fluconazole | Voriconazole |
| 1 (CBS 8973) | 16 (4) | 0.094 (0.125) | 32 | 0.50 |
| 2 (CBS 8975) | 32 (32) | 0.125 (0.125) | 128 | 0.25 |
| 3 (CBS 8969) | 24 (8) | 0.125 (0.125) | 64 | 0.25 |
| 4 (CBS 8971) | 24 (8) | 0.125 (0.25) | 64 | 1.00 |
| 5 (CBS 8970) | 24 (8) | 0.125 (0.125) | 64 | 0.50 |
| 6 (CBS 8972) | 32 (8) | 0.125 (0.125) | 64 | 0.25 |
| None (CBS 2479; type strain) | 24 (1) | 0.125 (0.25) | 64 | 0.25 |

[a] MICs as determined by the Etest system (AB Biodisk). Within parentheses are the MICs determined according to the NCCLS microbroth dilution method (5), which were defined as the lowest drug concentration at which there was complete absence of growth (MIC-0).

[b] The MFC was established as the lowest concentration of drug producing negative subcultures, after 20 μl of each clear well was plated on drug-free medium as described by Paphitou et al. (6).

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