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A Multicenter, double-blind trial of a high-dose caspofungin treatment regimen versus a standard caspofungin treatment regimen for adult patients with invasive candidiasis.

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BACKGROUND: The standard caspofungin treatment regimen (50 mg/day after a 70-mg dose on day 1) is effective and well tolerated for the treatment of invasive candidiasis, but experience with higher doses of caspofungin is limited. We evaluated the safety and efficacy of caspofungin at 3 times the standard dosing regimen.
METHODS: Patients with proven invasive candidiasis were randomized to receive a standard or high-dose (150 mg/day) caspofungin treatment regimen. Safety was assessed in all patients as treated. Efficacy was assessed as a secondary objective in a full-analysis-set population. A favorable overall response was defined as symptom resolution and microbiological clearance at the end of caspofungin therapy.
RESULTS: A total of 204 patients were included in the safety analysis (104 received the standard regimen, and 100 received the high-dose regimen), and 197 were included in the efficacy analysis (102 and 95 in the standard and high-dose treatment groups, respectively). Patient demographic characteristics, neutropenia status (6.7% and 8.0% had neutropenia, respectively), and Acute Physiology and Chronic Health Evaluation II scores (mean, 16.5 and 17, respectively) were similar between treatment groups. Significant drug-related adverse events occurred in 1.9% of patients receiving the standard regimen and 3.0% of patients receiving the high-dose regimen (difference, 1.1%; 95% confidence interval, -4.1% to 6.8%). The most-common drug-related adverse events in the standard and high-dose treatment groups were phlebitis (3.8% and 2.0%, respectively), increased alkaline phosphatase level (6.9% and 2.0%, respectively), and increased aspartate transaminase level (4.0% and 2.0%, respectively). Overall, 71.6% of patients who received the standard regimen and 77.9% of patients who received the high-dose regimen had favorable overall responses (difference, 6.3%; 95% confidence interval, -5.9% to 18.4%; not statistically significant). Mortality at 8 weeks after therapy was similar between groups.
CONCLUSIONS: Both caspofungin dosing regimens were effective and well tolerated in patients with invasive candidiasis. No safety concerns were found for caspofungin at a dosage of 150 mg/day. In other studies of invasive candidiasis, other antifungal agents have not demonstrated a higher success rate or improvement in survival relative to that found in the current study for caspofungin at the standard maintenance dosage of 50-mg/day. Overall, these results support the recommended standard dosing regimen for caspofungin. From a clinical perspective, this study provides important safety and efficacy data to guide prescribers who are considering a higher dose of caspofungin as part of a patient's treatment plan. Both the 50-mg and 150-mg dosing regimens for caspofungin treatment were effective and well tolerated in adult patients with invasive candidiasis. The results demonstrate a large safety margin for caspofungin, thereby allowing physicians the option of using higher-dose therapy if a demonstrated need arises.

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