Caspofungin Versus Amphotericin B for Candidemia: A Pharmacoeconomic Analysis

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ABSTRACT

Background: In a randomized, comparative, clinical trial, caspofungin was found to be as effective as amphotericin B deoxycholate (ampho B) for treating candidemia (favorable outcomes in 71.7% and 62.8% of patients, respectively) and exhibited a generally better safety profile, particularly with respect to impaired renal function (IRF) ($P = 0.02$).

Objective: The goal of this study was to examine whether cost savings generated from the reduced rates of IRF observed in the clinical trial would be enough to offset the higher acquisition cost of caspofungin relative to ampho B.

Methods: We developed an economic model in which 100 hypothetical patients with candidemia were treated with caspofungin or ampho B. Rates of IRF and duration of drug therapy were taken from the clinical trial. Information on the cost of treating IRF was obtained through a search of MEDLINE using the terms *amphotericin* and *cost, amphotericin* and *resource, amphotericin* and *hospital*, and *amphotericin* and *toxicity*; and the medical subject headings *kidney failure, acute/drug therapy; kidney failure, acute/epidemiology; kidney failure, acute/etiology; kidney/drug effects; cost of illness; costs and cost analysis; kidney failure, acute*, and *economics*; and *kidney failure, acute/economics*. In addition, the Web site www.doctorfungus.com was searched for relevant references, and the Merck publication alert system was used. Antifungal drug costs were estimated using data from IMS Health. Costs were reported in year-2003 US dollars.

Results: In the base case, the model projected that using caspofungin instead of ampho B would result in substantially lower treatment costs for IRF, which would more than offset the higher drug acquisition cost (cost-offset percentage, 122%), leading to a net mean savings of $758.60 per patient. These results were not very sensitive to the difference in daily drug cost, but were sensitive to the mean cost attributable to treating IRF. As that varied, the cost-offset percentage varied from 61% (substantial cost offset) to 183% (cost savings).

Conclusions: The results of this economic model suggest that, based only on differences in drug acquisition cost and renal toxicity, the use of caspofungin instead of ampho B in patients with candidemia may be a cost-saving strategy from the perspective of a hospital. (*Clin Ther.* 2005;27:960–969) Copyright © 2005 Excerpta Medica, Inc.

Key words: caspofungin, pharmacoeconomic analysis, amphotericin B, candidemia, cost-effectiveness.

INTRODUCTION

In a randomized, comparative, clinical trial, caspofungin was found to be as effective as amphotericin B deoxycholate (ampho B) for treating candidemia.[1] Additionally, caspofungin was shown to exhibit a generally better safety profile, particularly with respect to impaired renal function (IRF). By *IRF*, we are referring to what others have called *nephrotoxicity*[1–5] or *acute renal failure*.[3] In the clinical trial, a nephrotoxic effect was formally defined as at least a doubling of the serum creatinine level, or an increase of ≥1.0 mg/dL (88.4 mmol/L) if the baseline level was elevated.[1]

Summary of the Clinical Trial

Patients aged >18 years with ≥1 positive *Candida* culture from blood or another sterile site within the

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previous 4 days, plus signs of infection (including fever, hypothermia, hypotension, or signs of inflammation at a candida-infected site), were randomly assigned to blinded study drug, either caspofungin or ampho B.[1] Patients were to receive antifungal therapy for 14 days after the last positive culture, with a minimum of 10 days of IV therapy. Fluconazole could be substituted after 10 days if the clinical condition had improved, cultures had converted to negative for ≥48 hours, and neutropenia (if present) had resolved. Successful efficacy was defined as resolution of all symptoms and signs of infection and culture-confirmed eradication.

Baseline characteristics of the 2 groups were similar.[1] Risk factors included receipt of a transplant (3%), immunosuppressive therapy (21%), cancer (30%), hyperalimentation (42%), recent surgery (50%), central venous catheter (76%), and recent broad spectrum antibiotics (86%); multiple factors may have been present in individual patients. Of 239 patients enrolled, 224 were included in the modified intent-to-treat analysis (the primary analysis), which included patients with documented infection and who received ≥1 day of study drug. Duration of treatment was similar in the 2 groups: mean of 12.1 days and 11.7 days for caspofungin and ampho B, respectively (P = NS). A switch to fluconazole occurred in 25% and 35% of caspofungin and ampho B patients, respectively.

A favorable response occurred in 73.4% of patients treated with caspofungin and in 61.7% of patients treated with ampho B.[1] For patients with candidemia, a favorable outcome occurred in 71.7% and 62.8% of patients, respectively. Adverse events occurred more frequently in the ampho B group, including more frequent fever (P = 0.01), chills (P = 0.003), all clinical events (58.4% vs 28.9%, P = 0.002), and laboratory events in the aggregate (P = 0.002), including elevated blood urea nitrogen (P = 0.02), creatinine (P = 0.05), decreased potassium (P = 0.04), infusion-related events (49% vs 20%, P = 0.002), and nephrotoxicity defined as a rise in creatinine to twice the baseline value or an increase of ≥1 mg/dL in those with elevated baseline creatinine values (25% vs 8%, P = 0.02). Overall, there were more patients receiving ampho B than those who withdrew from the study due to an adverse event compared with caspofungin (23.2% vs 2.6%, P = 0.003). The authors concluded that caspofungin was as efficacious as ampho B, with less toxicity.[1]

Objective of the Current Work

IRF due to ampho B has been shown to be associated with increased morbidity, mortality, and use of health care resources.[2–6] Although the acquisition cost of caspofungin is more than that of ampho B (see "Methods"), using it instead of ampho B can be expected to reduce treatment costs attributable to IRF, as well as those attributable to other kinds of adverse events.[3,4,6] In this model analysis, we examined whether the cost savings generated from the reduced rates of IRF observed in the clinical trial would be enough to offset the higher acquisition cost of caspofungin relative to ampho B.

METHODS

Economic Model

We developed an economic model in which 100 hypothetical patients with candidemia were treated with caspofungin or ampho B. The model was structured as if one were considering the difference in hospital costs that would occur if caspofungin were used instead of ampho B. The perspective is that of a hospital, and the time horizon is short (1 week to a few months), consistent with the mean duration of antifungal treatment observed in the clinical trial (12 days, with a range of 1–28 days),[1] and the time associated with the treatment of acute renal toxicity.

Drug Acquisition Costs

Table I[1,7] illustrates how we estimated the difference in drug acquisition cost that would be observed if caspofungin were used instead of ampho B. We assumed daily doses consistent with those used in the clinical trial.[1] For caspofungin, this was 70 mg for the first day of therapy, followed by 50 mg/d thereafter. The dosing of ampho B varied from 0.6 mg/kg to 1.0 mg/kg per day, which translates to ranges of 36 to 60 mg for a 60-kg (132-lb) patient, 48 to 80 mg for an 80-kg (176-lb) patient, and 60 to 100 mg for a 100-kg (220-lb) patient. Given that our acquisition cost information for ampho B was based on 50-mg vials, we assumed that in 50% of the cases, 1 vial was used per day, and in the other 50%, 2 vials were used. Although it is possible that a patient could have weighed enough to receive >2 vials each day, we did not include that possibility in our analysis.

Mean acquisition costs for both antifungals were estimated using sales transaction data for nonfederal hospitals covering the period from July through

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