Cost-Effectiveness Analysis of Anti-Fungal Prophylaxis in Patients Undergoing Hematopoietic Cell Transplantation

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INTRODUCTION

Prophylaxis can decrease the incidence of fungal infections in transplant patients and lower the overall cost of care by reducing the number and cost of infections needing treatment. In a multi-center, blinded, randomized head-to-head comparative study evaluating the safety and efficacy of prophylaxis in 882 hematopoietic stem cell transplant (HSCT) patients, micafungin was shown to be more effective than fluconazole in preventing suspected fungal infection (84.9% vs 78.6%).

STUDY OBJECTIVE

An economic analysis was conducted to evaluate the cost-effectiveness of micafungin prophylaxis compared to fluconazole prophylaxis among patients undergoing HSCT.

METHODS

Cost-effectiveness measures were calculated to compare (1) prophylaxis with micafungin versus (2) prophylaxis with fluconazole. Efficacy data were taken from the clinical study, in which the incidence of proven or probable systemic fungal infections was 1.6% in the micafungin treatment arm and 2.4% in the fluconazole treatment arm. The percentage of patients receiving empiric therapy was 15.1% and 21.4% for micafungin and fluconazole, respectively. The economic analysis was conducted from the hospital perspective using costs incurred from admission through discharge. Each of the 882 patients was assigned costs and effectiveness based on their outcomes data from the clinical study. Published literature was used to estimate hospital costs (adjusted to 2005 values) associated with HSCT patients receiving prophylaxis, empiric anti-fungal treatment, and treatment for a probable or proven *Candida* or *Aspergillus* infection. Mean costs and effectiveness were calculated for each treatment group.

Table 1. Baseline analysis variables

Measure	Value
Cost of drugs for prophylaxis ($ per mg) [1]	
Micafungin	$2.24
Fluconazole	$0.12
Estimated hospital costs per HSCT patient [2,3]	
Successful empiric therapy	$153,379
Successful prophylaxis	$103,256
Proven fungal infection, candidiasis	$188,583
Proven fungal infection, aspergillosis	$248,632

Values adjusted to 2005 dollars. (Bureau of Labor Statistics, U.S. Department of Labor, CPI - All Urban Consumers, U.S. City Average, Hospital and Related Services)

[1] Red Book. Montvale, NJ: Medical Economics Co Inc; 2005.

[2] Cagnoni PJ, Walsh TJ, Prendergast MM et al. Pharmacoeconomic analysis of liposomal amphotericin B versus conventional amphotericin B in the empirical treatment of persistently febrile neutropenic patients. J Clin Oncol. 2000 Jun;18(12):2476-83.

[3] Wilson LS, Reyes CM, Stolpman M et al. The direct cost and incidence of systemic fungal infections. Value Health. 2002 Jan-Feb;5(1):26-34.

METHODS CONT'D

To test the variability of the results using repeated sampling, a bootstrapping analysis was also conducted, with 1,000 simulations of random samples of 100 patients from each treatment group. If appropriate to describe the results, incremental cost-effectiveness ratios were calculated, and sensitivity analyses were conducted by varying components of cost.

RESULTS

Mean cost for a course of prophylactic drug therapy was $2,018 for the 425 patients treated with micafungin and $843 for the 457 patients treated with fluconazole.

Table 2. Results of baseline analysis for HSCT

Measure	Micafungin (n=425)	Fluconazole (n=457)	Difference [1] in Average Costs and Effectiveness
Average costs			
Prophylactic drugs	$2,018	$843	$1,175
Hospital costs (other than prophylaxis)	$112,233	$116,978	-$4,745
Total hospital costs	$114,251	$117,821	-$3,570
SD	$21,025	$27,159	
Min	$103,480	$103,280	
Max	$248,969	$250,339	
Average effectiveness [2]	0.984	0.976	0.0076

[1] Positive (negative) dollar amounts indicate that micafungin costs are more (less) than fluconazole costs; positive effectiveness value indicates that micafungin is more effective than fluconazole.

[2] Effectiveness is assigned by the presence or absence of a proven fungal infection - with a fungal infection = 0 and without a fungal infection = 1.

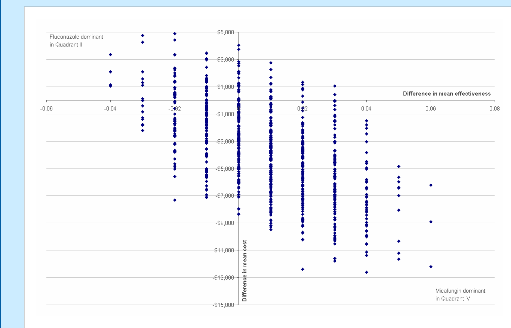
Incremental Cost-Effectiveness Ratio (ICER) [3] = **Micafungin Dominant** indicated by lower costs and greater effectiveness

[3] ICER obtained by dividing difference in total hospital costs by difference in average effectiveness.

Adding in other hospital costs, total patient costs were $114,251 and $117,821 for micafungin and fluconazole patients, respectively, a significant difference of $3,570 (p=0.015). Considering the lower rate of breakthrough fungal infection from the clinical study, micafungin is the dominant method of prophylaxis, with both lower costs and greater efficacy. The bootstrapping analysis indicated that micafungin prophylaxis was cost saving in 72.4% of the samples compared to 9.2% for fluconazole prophylaxis. Micafungin prophylaxis was dominant in 55.5% of the samples, compared to 6.4% for fluconazole prophylaxis.

RESULTS CONT'D

Figure 1. Scatterplot of bootstrapping analysis



The high concentration of results in Quadrant IV, where average costs are lower and average effectiveness is greater for micafungin, indicates the dominance of micafungin prophylaxis.

Sensitivity analyses on estimated hospital costs confirmed the superiority of micafungin as a cost-effective therapy.

Table 3. Results of sensitivity analysis for HSCT

Measure	Micafungin (n=425)	Fluconazole (n=457)	Total	Difference [1] in Average Costs
Baseline results				
Total hospital costs	$114,251	$117,821	$116,101	-$3,570
SD	$21,025	$27,159	$24,448	
Sensitivity analysis #1: Price per mg of micafungin increased by 50%				
Total hospital costs	$115,270	$117,821	$116,592	-$2,552
SD	$20,994	$27,159	$24,404	
Sensitivity analysis #2: Hospital costs of fungal infection = successful empiric therapy				
Total hospital costs	$113,530	$116,054	$114,838	-$2,524
SD	$18,550	$21,341	$20,073	
Sensitivity analysis #3: Hospital costs of empiric therapy = successful prophylaxis				
Total hospital costs	$106,821	$107,073	$105,542	-$251
SD	$12,219	$19,480	$16,379	

[1] Negative dollar amounts indicate that micafungin costs are less than fluconazole costs.

CONCLUSIONS

In addition to its greater efficacy, micafungin prophylaxis for patients undergoing HSCT leads to cost savings compared to fluconazole prophylaxis. Despite the higher costs of the drug itself, prophylaxis with micafungin reduces total hospital costs by $3,570 per patient, due to less need for empirical anti-fungal therapy and fewer proven or probable fungal infections.