Cost-effectiveness of posaconazole versus fluconazole for prevention of invasive fungal infections in US patients with graft-versus-host disease


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
This study examined the cost-effectiveness of posaconazole versus fluconazole, for the prevention of invasive fungal infections, in patients with graft-versus-host disease, after allogenic progenitor cell transplantation, in the USA. The authors concluded that posaconazole was a cost-effective alternative to fluconazole. The cost-effectiveness methods were transparent and valid. The authors' conclusions appear to be robust, but the analysis relied on the results of one clinical trial.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of posaconazole versus fluconazole, for the prevention of invasive fungal infections, in patients with graft-versus-host disease, after allogenic progenitor cell transplantation.

Interventions
The two antifungal preventive treatments were posaconazole and fluconazole. Oral posaconazole was given at 200mg three times daily and oral fluconazole was given at 400mg once daily. Each was administered for a maximum of 16 weeks or 112 days.

Location/setting
USA/hospital.

Methods
Analytical approach:
The decision model had a lifetime horizon. A decision tree simulated patient management for the 112 days of prophylaxis, and a Markov model, with one-month cycles, simulated their remaining lifetime. The authors stated that the perspective of the US payer was adopted.

Effectiveness data:
Most of the evidence was from a published multinational, randomised, double-blind, clinical trial of transplant recipients with grades two to four acute graft-versus-host disease, or extensive and chronic graft-versus-host disease, who were receiving intensive immunosuppression. This head-to-head trial provided data for the treatment effect and the patients' characteristics. Survival beyond the 16-week trial was estimated using published information and authors' assumptions. The efficacy of prophylaxis in preventing invasive fungal infection was the primary endpoint of the analysis.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
Life-years saved and invasive fungal infections avoided were the summary benefit measures. A 3% annual discount rate was used.
Cost data:
The economic analysis included the costs of antifungal prophylaxis and infection treatment. Prophylaxis was based on average prices for generic drugs. Treatment costs were from the Nationwide Inpatient Sample. Any charges were converted to costs using hospital-specific cost-to-charge ratios. All costs were in US $. The price year was 2006 and a 3% annual discount rate was applied.

Analysis of uncertainty:
Several one-way sensitivity analyses were carried out to assess the uncertainty around the key inputs for the model, using ranges mainly based on published confidence intervals or authors’ assumptions. A second-order probabilistic Monte Carlo simulation was performed, focusing on the key inputs, such as the probability of infection, the probability of death due to infection, the probability of death from other causes, and the treatment cost; conventional distributions were used.

Results
The rates of invasive fungal infection were 0.05 with posaconazole and 0.09 with fluconazole (OR 0.56, 95% CI 0.30 to 1.07). The expected discounted life-years were 7.87 with posaconazole and 7.66 with fluconazole. The total costs per patient were $8,860 with posaconazole and $5,710, with fluconazole.

The incremental cost per infection avoided with posaconazole over fluconazole was $85,300, and the incremental cost per life-year saved was $15,300.

The most influential inputs were the risk of an invasive fungal infection and the mean number of days of posaconazole. The incremental cost per life-year saved with posaconazole remained below $50,000 in every scenario. At a threshold of $50,000 per life-year saved, posaconazole was cost-effective in 90% of simulations (95% at a threshold of $100,000).

Authors’ conclusions
The authors concluded that posaconazole was a cost-effective alternative to fluconazole for the prevention of invasive fungal infections, in these patients.

CRD commentary
Interventions:
The selection of the comparators was appropriate as two of the available treatments for the prevention of invasive fungal infections were considered. The dosages were clearly reported.

Effectiveness/benefits:
The short-term clinical data were from a head-to-head randomised trial that should have had high internal validity, but no further details were given. The long-term data were from a published study with a 10-year time horizon, but again no further details were given. The authors conducted extensive sensitivity analysis to assess uncertainty around the many clinical parameters. A disease-specific and a generic benefit measure were used and combined with the costs. The use of life-years saved appears to have been appropriate for the patient population and allows comparisons with other disease interventions.

Costs:
The cost categories were appropriate for the perspective of the US payer. The cost items were not listed and the unit costs and resource quantities were not given, reducing the transparency of the analysis. The data sources were clearly reported and appear to have been consistent with the viewpoint of the payer. The costs were treated stochastically and appropriate distributions were assigned. The price year was reported, allowing reflation exercises. The impact of variations in the cost of invasive fungal infection treatment was assessed in the sensitivity analyses.

Analysis and results:
The results were clearly presented and an incremental analysis synthesised the costs and benefits of the alternative strategies. Normal cost-effectiveness thresholds were used to identify the optimal approach. Both deterministic and probabilistic sensitivity analyses were carried out to investigate uncertainty, and the methods and results were clearly reported and discussed. The authors acknowledged some limitations of their analysis, which mainly related to the lack
of long-term efficacy data and the need for some assumptions. The results appear to have been relevant to the authors’ context, but it was unclear whether they would be transferable to other settings.

Concluding remarks:
The cost-effectiveness methods were transparent and valid. The authors’ conclusions appear to be robust, but the analysis relied on the results of one clinical trial.

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