Economic evaluation of voriconazole for the treatment of candidemia in Canadian adults

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 voriconazole versus conventional amphotericin B followed by fluconazole for the treatment of candidemia. The authors concluded that voriconazole increased survival at day 98 and reduced toxicity, and might be a cost-effective strategy compared with a regime of intravenous conventional amphotericin B followed by fluconazole. Overall, the analysis was well reported and based on valid methodology. The authors’ conclusions appear to be appropriate.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to assess the cost-effectiveness of two strategies for the treatment of non-neutropenic patients aged 12 years and older and diagnosed with candidemia.

Interventions
The interventions were voriconazole (intravenous and oral) and a regime of intravenous conventional amphotericin B followed by fluconazole.

Location/setting
Canada/secondary care.

Methods
Analytical approach:
A decision analytic model with a time horizon of 98 days was used. The authors stated that the perspective of the health service, the Canadian Ministries of Health, was adopted.

Effectiveness data:
The effectiveness data were mainly obtained from a published randomised, double-blind, multinational phase III clinical trial; the Global Candidemia Study (Kullberg, et al. see ‘Other Publications of Related Interest’ below for bibliographic details). The parameters that were not available in the clinical study, such as switch treatment after discontinuation, dose and duration of switch therapy, duration of hospitalisation after discontinuation, and duration of mechanical ventilation, were based on the opinion of an expert panel consisting of ten physicians and two hospital pharmacists, who had experience in treating invasive fungal infections. The primary clinical outcome was cure, defined as mycological eradication and clinical treatment or improvement within 12 weeks after completion of therapy.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The authors used patient survival at 98 days as the primary measure of benefit. Further benefits combined with costs were the number of patients cured and the number of toxicities avoided.

Cost data:
The economic analysis included the costs of medications, diagnostic services, fungal screening, and mechanical ventilation. Resource use was either defined by the expert panel or based on data from the clinical trial. The costs were
derived from official Canadian sources, except for the cost of voriconazole, which was obtained from the pharmaceutical company (Pfizer, Canada Inc.). The unit costs and resource quantities were reported separately and all costs were reported in Canadian dollars (CAD).

Analysis of uncertainty:
Parameter uncertainty was investigated using one-way sensitivity analysis on the following model parameters: intensive care unit (ICU) costs, length of hospital stay for discontinuers, voriconazole vials per dose, monitoring costs, and mean weight for switch drug dose. Different scenario assumptions, were analysed, such as 100% of patients switched to a lipid formulation of amphotericin B, a time-horizon of 42 days, and 100% of patients discontinued initial treatment and switched to caspofungin. Probabilistic sensitivity analysis was performed using Monte Carlo simulation and cost-effectiveness scatter plots and a net-benefit acceptability curve were generated.

Results
The expected total average treatment costs were CAD 70,489 with voriconazole and CAD 69,368 with amphotericin and fluconazole. Giving an incremental average cost of CAD 1,121. The cure rates were equivalent in both treatment arms (41%). The proportion of patients surviving at day 98 was 64.52% with voriconazole and 58.20% with amphotericin and fluconazole, whilst the proportion of patients avoiding toxicity was 64.52% with voriconazole and 52.46% with amphotericin and fluconazole.

The incremental cost per additional patient surviving at day 98 was CAD 17,739 for voriconazole compared with amphotericin and fluconazole.

The results were most sensitive to variation in the time-horizon, ICU costs, and the additional hospital stay of discontinuers. The probabilistic sensitivity analysis demonstrated that voriconazole had a 88% probability for greater survival in day 98, but 49% probability of being cheaper than amphotericin and fluconazole. At a willingness-to-pay per additional life saved of less than CAD 20,000, voriconazole had less than 50% probability of being cost-effective.

Authors' conclusions
The authors concluded that voriconazole increased survival at day 98 and reduced toxicity, and might be a cost-effective strategy, for the treatment of candidemia, compared with a regime of intravenous conventional amphotericin B followed by fluconazole.

CRD commentary
Interventions:
The interventions were clearly reported and were chosen mainly with reference to a recent clinical trial. Alternative treatment options were available, but the authors stated that these were not analysed, due to a lack of relevant data.

Effectiveness/benefits:
The use of a double-blind, multinational randomised trial to derive the clinical data was appropriate, given the strengths of such a design. The details of this trial, such as the method of randomisation, inclusion and exclusion criteria, and power calculations, were not reported, which makes it difficult to objectively assess the validity of the data. There was some discussion around other economic studies, but it is not clear if other relevant clinical trials were available or were considered. Some estimates had to be obtained from expert opinion and, due to the uncertainty surrounding these data, extensive sensitivity analysis was conducted using wide ranges of values. Disease-specific benefit measures were used, which will not allow cross-disease comparisons, but may be more relevant for clinicians working within this field.

Costs:
The analysis of costs was consistent with the economic viewpoint. The sources of data were reported and unit costs and resource quantities were reported separately, increasing the transparency of the economic analysis. The authors highlighted the potential issue with protocol-driven resource use data and a more extensive one-way sensitivity analysis on these estimates would have been useful. The probabilistic analysis addressed some concerns surrounding parameter uncertainty. The price year was not explicitly reported, which prevents future reflation exercises.

Analysis and results:
The model structure, along with the modelling assumptions, was clearly reported. The costs and benefits were appropriately synthesised using an incremental approach. Overall, the issue of uncertainty was satisfactorily addressed, using deterministic as well as probabilistic analyses. The results of the base case and the sensitivity analysis were clearly reported. The authors acknowledged some limitations to their study. The reporting was transparent, with all assumptions clearly outlined allowing any limitations of the analysis to be clearly judged.

Concluding remarks:
Overall, the analysis was well reported and based on valid methodology. The authors’ conclusions appear to be appropriate.

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