Comparative cost-effectiveness of voriconazole and amphotericin B in treatment of invasive pulmonary aspergillosis

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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 amphotericin B in the treatment of invasive pulmonary aspergillosis in patients with and without a halo sign at thoracic computed tomography scan. The authors concluded that voriconazole resulted in survival gains and was likely to be cost-effective. The methodology was appropriate and transparently reported, but more details about the clinical evidence would have been useful. The authors' conclusions seem to be appropriate.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to examine the comparative cost-effectiveness of voriconazole versus amphotericin B in the treatment of invasive pulmonary aspergillosis (IPA) in two subgroups of patients, those with and without a halo sign at thoracic computed tomography (CT) scan.

Interventions
The interventions were a 12-week treatment with voriconazole or amphotericin B.

Location/setting
USA/hospital.

Methods
Analytical approach:
This economic evaluation was based on a decision model which relied on data from a single study. The time horizon of the analysis was 12 weeks. The authors stated that the perspective was that of society.

Effectiveness data:
The clinical data were derived from the published Global Comparative Aspergillosis trial, with a follow-up period of 12 weeks. Only those patients with a CT scan at baseline were included (118 of 144 in the voriconazole group, and 104 of 133 in the amphotericin B group). In the subgroup of patients with a halo sign, there were 77 in the voriconazole group and 66 in the amphotericin B group. In the subgroup of patients without a halo sign, there were 41 in the voriconazole group and 38 in the amphotericin B group. The primary outcome of the clinical analysis was patient survival at 12 weeks.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The 12-week survival rate was the summary benefit measure, which was derived from the clinical trial and the decision model.

Cost data:
The analysis considered the costs of antifungal treatment, hospital intensive care, stay in regular wards, hospital or
outpatient clinic visits, outpatient visits to a specialist, and outpatient visits to a general practitioner. The unit costs and quantities of resources used were presented separately. The resource use data were derived directly from the clinical trial and collected prospectively. The costs were derived from official US sources such as the Red Book, the Healthcare Cost and Utilization Project (HCUP), and the Centers for Medicare and Medicaid Services. Diagnosis-related group-specific cost to charge ratios were applied when required. All costs were in US dollars ($) and the price year appears to have been 2004.

Analysis of uncertainty:
The issue of uncertainty was investigated primarily by means of a Monte Carlo simulation, which assigned probabilistic distributions to the model inputs in order to generate cost-effectiveness acceptability curves. A deterministic univariate sensitivity analysis considered alternative values for the resource use data (the ranges of which were based on the standard errors derived from the clinical trial), hospital costs (which were derived from the Michigan HCUP), and the unit costs of all antifungal therapies (which were varied by plus and minus 20% their baseline values).

Results
In patients with a halo sign, the mean cost per patient was $40,380 with voriconazole and $48,985 with amphotericin B. The 12-week survival rates were 75% and 65%, respectively. Thus, voriconazole was the dominant treatment (both more effective and less expensive).

In patients without a halo sign, the mean cost per patient was $48,133 with voriconazole and $45,938 with amphotericin B. The 12-week survival rates were 66% and 40%, respectively. The incremental cost per additional survivor with voriconazole over amphotericin B was $8,321.

The deterministic sensitivity analysis confirmed the dominance of voriconazole in patients with a halo sign. In those without a halo sign, the maximum incremental cost-effectiveness ratio was $11,835 in the worst-case scenario.

The probabilistic analysis suggested that the probability of voriconazole being cost-effective was over 95% in patients with a halo sign and over 50% for threshold values above $8,000 per additional 12-week survivor in patients without a halo sign.

Authors' conclusions
The authors concluded that, in patients with IPA, initiating treatment with voriconazole rather than with amphotericin B resulted in survival gains and was likely to be cost-effective.

CRD commentary
Interventions:
The authors did not provide an explicit justification for their selection of the interventions, but they were the comparators in the clinical trial.

Effectiveness/benefits:
The clinical evidence was derived from a randomised controlled trial, which is usually considered to be a good source of evidence due to the strengths of its design. However, the authors only reported a few methodological features of the study. They stated that the subgroups were very small samples, which may not have had sufficient power to capture significant differences between the treatment groups, and which may have reduced their baseline comparability. Thus, it is not possible to judge how robust and valid the clinical data were. The derivation of the benefit measure was appropriately based on the model framework. However, such a measure might not be directly comparable with the benefits of other health care interventions, especially because it was restricted to a very short time horizon, which precluded the calculation of long-term survival, as the authors acknowledged.

Costs:
The analysis of costs was restricted to the viewpoint of the health care system although the authors stated that a societal perspective was adopted. In general, the economic analysis was carried out transparently. The steps in the calculation of hospital costs were clearly reported. The sources of data, unit costs, quantities of resources used, price year, use of statistical tests, cost adjustment techniques, and use of alternative assumptions were described in detail. These aspects...
enhance the validity of the economic analysis.

Analysis and results:
The synthesis of the costs and benefits was appropriately carried out using average and incremental ratios. The issue of uncertainty was satisfactorily addressed in the sensitivity analyses, which were clearly described and the findings of which were extensively reported and discussed. The issue of generalisability was not investigated and the results might not be transferable to other settings. However, the authors compared their results with those of other published studies showing similar findings.

Concluding remarks:
The methodology appears to have been appropriate and was clearly and transparently reported, but more details about the clinical evidence would have been useful. The authors’ conclusions seem to be appropriate.

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