Cost-effectiveness evaluation of voriconazole versus liposomal amphotericin B as empirical therapy for febrile neutropenia in Australia

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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 investigated the costs and clinical outcomes of two anti-fungal medications, liposomal amphotericin B (LAMB) and conventional voriconazole, for patients with febrile neutropenia. The authors concluded that LAMB had clinically superior outcomes and net cost-savings compared with voriconazole. The effectiveness of LAMB appears to be valid, the costing methods and results were fully transparent, and the authors’ conclusions appear to be reasonable.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to assess the costs and health effects of using voriconazole versus liposomal amphotericin B (LAMB) as prophylactic anti-fungal treatment for febrile neutropenia. The study population comprised adults with a mean body weight of 76.05kg.

Interventions
Voriconazole at an intravenous dose of 6mg per kg twice on the first day, followed by oral 200mg tablets twice daily, was compared with LAMB at an intravenous dose of 3mg per kg per day throughout treatment. Higher doses were given if patients had baseline fungal infections, which were those diagnosed within 24 hours of initiation of treatment.

Location/setting
Australia/out-patient care.

Methods
Analytical approach:
The economic evaluation was undertaken retrospectively and was based on a single, multi-centre, clinical trial (Walsh, et al. 2002, see ‘Other Publications of Related Interest’ below for bibliographic details). A decision analytic model was constructed and clinically validated. The authors reported that the study was carried out from the Australian hospital perspective.

Effectiveness data:
The primary clinical outcome was treatment success, which was defined as an individual having no breakthrough fungal infections (diagnosed after 24 hours of treatment), surviving beyond seven days, not discontinuing therapy, and having resolution of fever and any baseline fungal infection. Secondary outcomes were morbidity, mortality, duration of initial therapy, and reasons for treatment failure. The clinical data were derived from a single, prospective, randomised double-blind clinical trial (Walsh, et al. 2002) with a sample of 837 patients.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The measure of benefit was treatment success, as defined above.

Cost data:
The resource types included drug therapy, concomitant antibiotics, screening and monitoring tests for fungal infections, and intensive care unit (ICU) stays. A panel of four expert Australian clinicians were employed to provide the estimates of treatment resources, therapy duration, and side-effect implications. The value of medications was from their wholesale prices (those paid by Australian public hospitals), hospitalisations were valued from 2006 to 2007 Australian Refined Diagnosis-related group data, and ICU bed cost was from a published source. All the unit costs were reported in 2007 to 2008 Australian dollars (AUD) and adjusted, where necessary, using the Australian Consumer Price Index.

Analysis of uncertainty:
One-way, two-way, and probabilistic sensitivity analyses were used to examine how the uncertainty in the modelled inputs impacted on the final results. Triangular distributions were used for all clinical inputs in the probabilistic sensitivity analysis. The sensitivity results were illustrated in a tornado diagram and cost-effectiveness acceptability curves.

Results
The mean cost per patient was AUD 49,237 for voriconazole and AUD 47,815 for LAMB with a net cost-saving of AUD 1,422 in favour of LAMB. A higher probability of success was found for LAMB (30.57%) than for voriconazole (26.02%). Similarly, a lower probability of death was associated with LAMB (5.92%) than with voriconazole (7.95%).

The cost per patient successfully treated with LAMB was AUD 32,816 lower than that with voriconazole. Overall, LAMB was found to be dominant over voriconazole as it had higher clinical efficacy and lower costs.

Sensitivity analyses showed that the duration of therapy was the most important cost driver. The costs for voriconazole were lower than those for LAMB, when LAMB therapy duration was more than 10.4 days, or when voriconazole therapy duration was less than 9.6 days. There was a 99.8% likelihood that LAMB would produce net cost-savings over voriconazole.

Authors' conclusions
The authors concluded that LAMB was dominant over voriconazole in the first-line empirical treatment of anti-fungal infections for patients with febrile neutropenia, as it produced more successfully treated patients at a lower overall cost.

CRD commentary
Interventions:
The two intervention groups were fully described and the expert panel confirmed that these anti-fungal doses and regimens reflected the usual clinical practice in Australia. Readers should decide if these options are feasible in their own settings.

Effectiveness/benefits:
The effectiveness data were based on a rigorous, randomised, controlled, multi-centre trial. As limited data on this trial were reported, readers are referred to the trial publication (Walsh, et al. 2002) for further information on the analytical approaches, statistical power, patient characteristics, and internal validity of the clinical findings. The trial is likely to have produced high-quality evidence for the effectiveness estimates.

Costs:
There was detailed reporting of the costing methods including the types of costs, their measurement, the unit costs, and the analyses. The analytical time frame was short-term, but its length was not defined. The types of costs appear to have accurately reflected the hospital perspective, with the exception that the costs for treating the common side-effects of anti-fungal drugs were omitted. In the absence of complete data on resource use, an expert clinical panel was used to inform resource use, confirm the local conditions, and validate the model structure.

Analysis and results:
The base-case results were clear and the sensitivity analysis results were comprehensively reported and illustrated. Discounting was not relevant due to the short time horizon. The authors acknowledged the following limitations of their study. The results might not generalise to other countries where conditions may differ; some simplifications were made in the model structure, such as only one switch to an alternative therapy allowed due to side-effects; and an expert panel...
was used when no other data were available.

Concluding remarks:
The clinical effectiveness results and costing methods were comprehensive and valid. The authors’ conclusions are likely to reflect the scope of the economic analysis undertaken.

Funding
Funded by the Monash Graduate Scholarship, Monash University.

Bibliographic details

PubMedID
19001450

DOI
10.1093/jac/dkn459

Original Paper URL
http://jac.oxfordjournals.org/cgi/reprint/63/1/197

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Amphotericin B /economics /therapeutic use; Australia; Cost-Benefit Analysis; Fever; Humans; Mycoses /complications /drug therapy; Neutropenia; Pyrimidines /economics /therapeutic use; Treatment Outcome; Triazoles /economics /therapeutic use; Voriconazole

AccessionNumber
22009100452

Date bibliographic record published
06/05/2009

Date abstract record published
03/02/2010