Cost-effectiveness analysis comparing liposomal anthracyclines in the treatment of AIDS-related Kaposi's sarcoma


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.

Health technology
Liposomal anthracyclines in the treatment of AIDS-related Kaposi's Sarcoma (KS).

Type of intervention
Treatment

Economic study type
Cost-effectiveness analysis.

Study population
The study population was severely immunocompromised HIV-infected individuals with a mean CD4 T-lymphocyte count of 30. Approximately 22% of patients had pulmonary KS.

Setting
The practice setting was a secondary care institution; the economic study was performed in the United States.

Dates to which data relate
Effectiveness and resource use data were derived from two studies published in 1996 and 1998. The price year was not stated.

Source of effectiveness data
The evidence for clinical response and toxicity results was based on a review of previously completed studies.

Modelling
A decision-analysis model was used to estimate the costs and cost-effectiveness of the two liposomal formulations. The model was used to estimate costs from clinical outcomes and resource use data derived from published phase III clinical studies.

Outcomes assessed in the review
Clinical response and toxicity results were assessed in the review.

Study designs and other criteria for inclusion in the review
Randomised phase III trials comparing liposomal anthracyclines with standard systemic chemotherapy (such as bleomycin and vincristine (BV) or bleomycin/vincristine and doxorubicin (ABV) were identified. Response rates had to
be measured in an equivalent manner including both complete and partial responses according to criteria defined by the AIDS Clinical Trial Group. Results from studies that would not allow proper comparison between the two agents because of differences in clinical response criteria were not included.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
Not stated.

**Methods used to judge relevance and validity, and for extracting data**
The judgement criteria were not stated. Summary statistics from each study were used to extract data.

**Number of primary studies included**
Two primary studies were included in the review. Both were randomised phase III clinical trials.

**Methods of combining primary studies**
Combination was not required as there was only one study for each of the two agents.

**Investigation of differences between primary studies**
The authors reported that the pegylated liposomal doxorubicin study defined duration of response as the number of days from onset of the response to the first evaluation of either stable disease or progressive disease. The liposomal daunorubicin study defined this value as the number of days from onset of the response to the first evaluation of progressive disease.

**Results of the review**
Among severely immunocompromised patients with KS who received pegylated liposomal doxorubicin or liposomal daunorubicin in separate randomised controlled trials, the complete and partial response rates were 59% and 25%. The median duration of response was 142 days versus 175 days.

**Measure of benefits used in the economic analysis**
Partial or complete response was the outcome measure used in the economic analysis.

**Direct costs**
Quantities and costs were reported separately. Direct costs to the health service were included in the analysis. The costs estimated were for the full course of the specified chemotherapy, assuming this was the only therapy patients received and that any further treatment costs would be identical across the groups. The estimation of quantities was based on actual data whilst the estimation of costs was based of data derived using a modelling study. Costs of liposomal anthracyclines were based on average US wholesale prices, plus an estimated administration cost for intravenous fluid administration and nurse monitoring. It was assumed that gastrointestinal toxicities were equivalent and that more than 90% were grades I/II, thus requiring no significant use of antiemetics. Costs were not discounted because of the short time frame of the study.

**Indirect Costs**
Indirect costs were not included.
Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were performed to evaluate the extent to which the estimated cost-effectiveness results varied given alternative assumptions. Analyses were performed based on parameters from published phase II and III trials, with variance in clinical and resource estimates of response rates (+/-10%), rates of growth factor use (+/-6%), costs of treatment of febrile neutropenia (an additional $300/responder) and dosage regimen. A comparison was also made using both higher dose and higher efficacy for liposomal daunorubicin and using an assumption of six cycles of treatment for both strategies.

Estimated benefits used in the economic analysis
Among severely immunocompromised patients with KS who received pegylated liposomal doxorubicin or liposomal daunorubicin in separate randomised controlled trials, the complete and partial response rates were 59% and 25%.

Cost results
The total cost/patient was $6,621 for liposomal daunorubicin versus $7,066 for pegylated liposomal doxorubicin. The difference in costs was associated with longer cycle length and fewer average treatment cycles, and fewer episodes of grade III/IV neutropenia for pegylated liposomal doxorubicin, which were offset by higher acquisition costs per cycle ($1,212 versus $538).

Synthesis of costs and benefits
Cost-effectiveness estimates favoured pegylated liposomal doxorubicin, which cost $11,976 per responder, compared to $26,483 per responder for liposomal daunorubicin. This reflected the difference in response rates in the clinical trials. The marginal cost-effectiveness for pegylated liposomal doxorubicin was determined to be $1,308 per additional responder. This demonstrates that the incremental efficacy of pegylated liposomal doxorubicin over liposomal daunorubicin can be achieved at very low incremental cost.

Sensitivity analyses showed that these results held over a wide range of estimates for clinical use and economic outcomes.

Authors' conclusions
The average cost-effectiveness of therapy for advanced AIDS-related KS favours the use of pegylated liposomal doxorubicin. In addition, the marginal cost-effectiveness ratios for liposomal doxorubicin show only a small incremental cost to gain additional responders, particularly compared with the overall cost of care for these patients.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparators used (standard systemic chemotherapy, such as bleomycin and vincristine (BV) or bleomycin/vincristine and doxorubicin (ABV)). You should consider whether these are widely used health technologies in your own setting.

Validity of estimate of measure of benefit
The effectiveness evidence was derived from two randomised phase III clinical trials. As they were not head-to-head trials, modelling was used to combine the findings of the two RCTs in order to estimate the cost-effectiveness of the two liposomal formulations. The authors listed a number of factors that may have affected the estimate of the measure of benefit used in the study. Firstly, the treatment regimens for the two liposomal agents differed (with respect to dose and schedule). Secondly, undocumented clinical characteristics may have differed and finally, it is uncertain how
carefully the ACTG criteria were applied and how much this varied between studies.

**Validity of estimate of costs**
Resource quantities were reported separately from prices and adequate details of quantity/cost estimation were given. The cost analysis was performed from a health service perspective and therefore costs to patients and others in society were not included.

**Other issues**
The issue of generalisability to other settings was addressed with the authors pointing out that costs and outcomes in clinical practice settings can differ from those associated with clinical trials. The authors also indicated that the response rates for standard combination therapy (BV and ABV) were lower than those previously reported in the literature, ranging from 57% to 88%.

**Implications of the study**
Well-designed trials with direct comparison of doxorubicin and daunorubicin in the treatment of AIDS-related Kaposi’s Sarcoma are needed. In these quality of life issues can also be taken into consideration.

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**Bibliographic details**

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
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