Cost-effectiveness analysis comparing chemotherapy regimens in the treatment of AIDS-related Kaposi's sarcoma in Brazil
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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.

Health technology
The study examined several palliative regimens for Kaposi's sarcoma (KS) related to acquired immunodeficiency syndrome (AIDS). The regimens considered were pegylated liposomal doxorubicin (PLD), liposomal daunorubicin (DNX), and a combination of doxorubicin, bleomycin and vincristine (ABV). Assumed dosages were 20 mg/m2 every 2 weeks for PLD and 40 mg/m2 every 2 weeks for DNX. ABV was given as doxorubicin 20 mg/m2, bleomycin 10 mg/m2 and vincristine 1 mg every 2 weeks, or as doxorubicin 10 mg/m2, bleomycin 15 mg/m2 and vincristine 1 mg every 2 weeks.

Type of intervention
Palliative care.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients with severe immunocompromised AIDS-related KS (CD4 cell count <50 cells/microL) who require chemotherapy as palliative care.

Setting
The setting was a hospital. The economic study was carried out in Brazil.

Dates to which data relate
Clinical data and information on resource consumption were derived from studies published in 1996 and 1998. The price year was 2004.

Source of effectiveness data
The clinical data used in the analysis were the partial or complete response rate to chemotherapy agents (effectiveness), and toxicity requiring the use of colony-stimulating factors (CSFs).

Modelling
The authors stated that a decision analysis model was developed. However, it appears that this model referred to the general framework of a cost-effectiveness analysis rather than an analytic model, no details of which were reported.

Sources searched to identify primary studies
The clinical data were derived from two randomised clinical trials (RCTs), which were both carried out in the USA.
The sample size of both studies was reported. Further, the authors reported the mean CD4 cell count at baseline of the patients enrolled in the studies and the key study results. The two Phase III studies evaluated DNX versus ABV and PLD versus ABV.

Methods used to judge relevance and validity, and for extracting data
The two studies appear to have been identified selectively rather than through a systematic review of the literature, the intention being to obtain the most recent and valid sources of data. The authors stated that they used the most recent data for PLD. Some assumptions about gastrointestinal toxicity and frequency of opportunistic infections were also made.

Measure of benefits used in the economic analysis
The summary benefit measure was the response rate. This was derived directly from the published RCTs. No discounting was necessary.

Direct costs
The viewpoint of the analysis was that of the Brazilian public health system. The cost categories included in the analysis were chemotherapy drugs, their administration and the treatment of haematopoietic toxicities. The unit costs and resource quantities were not presented separately. Data on resource consumption were derived directly from the two RCTs. The costs of drugs were based on Brazilian retail sale prices. Other medical costs came from the Ministry of Health - Health Prices Database in 2004. Drug administration costs were estimated using data from the management department of the authors' university hospital in Ribeirao Preto, and included costs of average day-care facilities visits (personnel salaries, materials and hospital maintenance expenses). The costs of CSF were based on a 5-day course of filgrastim. Discounting was not relevant given the short time horizon of the analysis, arising from the poor survival of patients. The price year was 2004.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
Productivity costs were not considered.

Currency
Brazil reais (BRL) converted in US dollars ($). The average exchange rate for 2004 was used (although not reported).

Sensitivity analysis
A univariate, deterministic sensitivity analysis was performed to evaluate the robustness of the cost-effectiveness ratios to variations in response rate (+ 13% for DNX), acquisition cost of chemotherapy agents (-5% for PLD), rates of CSF use (+/- 6%) and dosage regimen (changes in cycles and increase in dosage for DNX). Alternative values were either set by the authors or derived from the literature.

Estimated benefits used in the economic analysis
The response rate was 46% with PLD, 25% with DNX and 25% with ABV in the study in which ABV was compared with PLD. The response rate was 28% in the study in which ABV was compared with DNX.

Cost results
The expected cost per patient was $4,725 with PLD, $4,065 with DNX and $317 with ABV in the study in which ABV was compared with PLD.
was compared with PLD. The expected cost was $395 per patient in the study in which ABV was compared with DNX.

**Synthesis of costs and benefits**

Average and incremental cost-effectiveness ratios were calculated in order to combine the costs and benefits of the alternative strategies.

The average cost per patient who responded completely or partially to therapy was $1,268 with ABV in the study in which ABV was compared with PLD (only estimate provided for ABV), $16,260 with DNX and $10,271 with PLD.

The incremental cost per additional patient who responded completely or partially was $20,990 for PLD in comparison with ABV and $3,142 for PLD in comparison with DNX.

The results of the sensitivity analysis did not substantially alter the base-case findings. In general, PLD showed a better cost-effectiveness profile than DNX.

**Authors’ conclusions**

Pegylated liposomal doxorubicin (PLD) had a better cost-effectiveness in comparison with liposomal daunorubicin (DNX). However, the combined doxorubicin, bleomycin and vincristine (ABV) regimen represents a reasonable treatment option for acquired immunodeficiency syndrome (AIDS)-related Kaposi’s sarcoma (KS) in a resource-poor setting such as Brazil, owing to its low acquisition cost in comparison with liposomal anthracyclines.

**CRD COMMENTARY - Selection of comparators**

The authors justified their choice of the comparators, which were appropriate. They stated that combination therapy using vincristine and bleomycin, with or without doxorubicin, was considered to be the standard chemotherapy regimen for AIDS-KS in resource-poor settings, but that these strategies have been supplanted by liposomal anthracyclines on the grounds of their higher efficacy and lower toxicity. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**

The few clinical data used in the analysis were derived from two selectively identified RCTs. RCTs usually have a high internal validity, thus ensuring the validity of the clinical data. The authors provided some details about the two studies, which help in judging the robustness of the clinical information. The lack of a systematic search for published data may have been justified, as the authors intentionally selected the most recent and reliable evidence on the effectiveness of the chemotherapy regimens. The authors noted that the evidence for the two liposomal anthracyclines was based on an indirect comparison, owing to the lack of head-to-head RCTs.

**Validity of estimate of measure of benefit**

The benefit measure was specific to the disease considered in the study and would not be comparable with the benefits of other health care interventions. The response rate was derived from the literature. Changes in the response rate were investigated in the sensitivity analysis.

**Validity of estimate of costs**

The analysis of the costs was consistent with the authors’ stated perspective. No information on the unit costs and resource quantities was given, which will limit the possibility of replicating the analysis in other settings. The authors excluded the costs of chemotherapy pre-medication and of treating infections on the grounds that they were likely to be similar between groups. Statistical analyses were not performed, but some cost items were varied in the sensitivity analysis. The sources of the data were reported for all categories and were consistent with the viewpoint of the analysis. The price year was reported, thus facilitating reflation exercises in other time periods.

**Other issues**

The authors did not compare their findings with those from economic evaluations carried out in industrialised countries, owing to the differences in the setting of the analysis. The issue of the generalisability of the study results to other
settings was partially addressed in the sensitivity analysis. The authors pointed out that the use of data from US patients applied to the Brazilian epidemiological context may be a limitation of the analysis. Further, it was noted that duration of response is a key aspect of the analysis that was not taken into account. A further drawback of the study was the fact that the analysis did not consider the use of highly active antiretroviral therapy (HAART) in addition to chemotherapy since this strategy was not evaluated in the two RCTs.

**Implications of the study**
The study results suggest that ABV might represent a cost-effective strategy for the palliation of patients with AIDS-KS. Future studies should investigate the cost-effectiveness of HAART in addition to chemotherapy.

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None stated.

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**Other publications of related interest**
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**Indexing Status**
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