Analysis of the cost-effectiveness of paclitaxel as alternative combination therapy for advanced ovarian cancer

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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
Paclitaxel combined with cisplatin as a therapy for advanced ovarian cancer.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Women with stage III and stage IV epithelial carcinoma of the ovary.

Setting
Hospital. The economic study was carried out in New York, USA.

Dates to which data relate
The effectiveness and some resource use data were derived from a study published in 1996. The remaining data on resource use were obtained from a panel of practising clinical oncologists with no reference date reported for their calculations/opinions. The costs were reported using 1996 prices.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken based on prospective data collected on the patient sample used in the effectiveness study.

Study sample
A total of 386 patients was included in the study. Of these, 202 patients were allocated to the CP group (cyclophosphamide 750 mg per square metre and cisplatin 75 mg per square metre of body surface area), whilst 184 patients were assigned to the TP group (paclitaxel 135 mg per square metre over a period of 24 hours and cisplatin as before). Power calculations were not reported.

Study design
The study was a randomised controlled trial conducted in at least 39 different institutions. The patients were allocated
by stratification according to the institution and the clinical measurability of disease. The median duration of follow-up was 37 months (range: 5 - 56).

Analysis of effectiveness
The analysis was based on intention to treat. Primary outcomes were response rate, adverse reaction incidence (using the toxicity severity criteria of the Gynecologic Oncology Group, based on all those patients with at least one course of treatment; of those randomised, only one patient was excluded from the analysis) and survival duration. Those having a complete response and those without a measurable disease, underwent a reassessment laparotomy to determine the pathological response. Progression-free survival was also analysed. The groups were comparable in terms of age, Gynaecologic Oncology Group performance status, cell type, tumour grade, measurability of disease, stage and presence of ascites (>100 ml). Groups were also comparable in terms of the total planned (450 mg per square metre) and delivered dose of cisplatin.

Effectiveness results
For those 216 women with measurable disease, 73% in TP and 60% CP responded to therapy, (p=0.01). The laparoscopic reassessment showed no difference (20% and 26%, p>0.05) between treatment arms in terms of complete response. The median survival was 38 and 24 months, respectively for the TP and CP groups (p<0.001). Progression-free survival was 18 months for the TP and 13 months for the CP group, (p<0.001). The frequency of grade 4 neutropenia (the most severe) was 78% and 61% in the TP and CP, respectively, (p<0.05 for test of overall difference in severity between groups). Alopecia, fever and allergic reactions were also observed more frequently in the TP group (p<0.05 for test of overall difference in severity between groups). The mean survival duration was estimated to be 2.03 years in the CP group and 3.13 years in the TP group.

Modelling
An economic model was used to determine whether the alternative paclitaxel-cisplatin (TP) therapy was cost-effective in comparison to standard cyclophosphamide-cisplatin (CP) therapy. The model was based on the recommendations of a panel of practising clinical oncologists who compared the clinical trial resource use with resource use patterns of a 'real world' situation. Thus, they characterised adverse reaction treatment regimens and resource use consumption in general. The costing exercise assumed an administration of six full cycles of therapy. A Monte Carlo simulation was used to analyse the robustness of the estimates to variation in the data.

Measure of benefits used in the economic analysis
The measure of benefits was life years gained. The corresponding estimates were derived from the actual data (means) from the effectiveness study. No account was taken of the effects on benefits of adverse reactions to treatment.

Direct costs
Total drug acquisition, facility, adverse event management and follow-up therapy costs for CP and TP were included in the analysis. The costing was based on a 'real world' scenario of resource use as determined from the recommendations of an expert panel of five practising clinical oncologists who compared clinical trial data on resource use corresponding to the effectiveness study with general practice patterns of resource use. An activity-based costing approach was used in valuing costs using the Resource Based Relative Value Schedule (RBRVS) and drug acquisition costs derived from the Oncology Therapeutics Network (OTN) programme. Quantities of resource use associated with drug therapy (chemotherapy drug and concomitant medication) and adverse reaction management were analysed separately from costs. Costs were discounted. The quantity/cost boundary adopted was that of the hospital. The date of the price data was 1996.

Currency
US dollars ($).
Sensitivity analysis
A one-way and multi-way sensitivity analysis was performed on different input values. Monte Carlo simulations were used to analyse the effect on the results of variation in the underlying data.

Estimated benefits used in the economic analysis
The survival duration was estimated to be 2.03 years in the CP group and 3.13 years in the TP group (means from the effectiveness study; source: authors' statement in the economic evaluation study).

Cost results
In an inpatient setting, the per patient cost of TP and CP was $29,824 and $21,086, respectively. Therefore, the incremental cost of TP with respect to CP was $8,737.34. The corresponding figures for the outpatient setting were $27,320 and $17,964, for an incremental per patient cost of $9,335.21 for TP relative to CP. An annual discount rate of 4% was used in the above estimates of costs.

Synthesis of costs and benefits
Using 1996 prices and a 4% discount rate for costs, the incremental costs per year of life gained (YLG) under TP therapy was estimated to be $19,820 and $21,222 for the inpatient and outpatient treatments, respectively. The sensitivity analyses showed the results to be robust to variation in the main parameters of the analytical framework.

Authors' conclusions
The TP regimen's increased mean survival cost per YLG (inpatient and outpatient settings) adds a substantial benefit at an acceptable cost compared with CP therapy. TP is a cost-effective alternative to the standard therapy for advanced ovarian cancer.

CRD COMMENTARY - Selection of comparators
The reason for the choice of comparator is clear. Cyclophosphamide-cisplatin (CP) was the standard therapy of choice in the treatment of advanced ovarian cancer.

Validity of estimate of measure of benefit
Note that benefits (life years gained by the intervention relative to the standard) were not discounted even though costs were. The effectiveness study underlying the estimate of benefit is a large, well conducted study with associated data and results likely to be valid. Note that the authors chose the more conservative estimate of benefit of mean survival rather than median survival; the implied difference was 0.066 years (i.e. 24 days). Note also that the increased frequency of adverse reactions associated with TP was not included in the estimation of benefits, only in the cost estimation (see below).

Validity of estimate of costs
Some resource use quantities were reported separately from the costs. Adequate details of methods of quantity/cost estimation were given. No important cost items seem to have been omitted from the analysis (costs of adverse reactions leading to health care resource use were included in the estimates of total costs).

Other issues
The authors' conclusions were justified based on the sensitivity analyses. The issue of generalisability to other settings was partly addressed. Appropriate comparisons were not made with other studies. The results were not presented selectively, although it should be noted that benefits were not discounted whereas costs were.
Implications of the study
Further analysis of the data and information on resource use would be desirable in order to allow the reader a clearer picture about the generalisability of the study results of this well-conducted study.

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