Management of platinum-sensitive recurrent ovarian cancer: a cost-effectiveness analysis
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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 three chemotherapy regimens for patients with recurrent platinum-sensitive ovarian cancer: carboplatin alone (C), paclitaxel plus carboplatin (PC), and gemcitabine plus carboplatin (GC).

C consisted of carboplatin at an area under the curve (AUC) of 5 administered on day 1 of a 21-day cycle.

PC consisted of paclitaxel at 175 mg/m2 followed by carboplatin at an AUC of 5 administered on day 1 of a 21-day cycle.

GC consisted of 1,000 mg/m2 intravenous gemcitabine administered on days 1 and 8 of a 21-day cycle, as well as carboplatin at an AUC of 4 administered on day 1.

Type of intervention
Palliative care.

Economic study type
Cost-effectiveness analysis

Study population
The study population comprised a hypothetical cohort of women with platinum-sensitive ovarian cancer recurring more than 6 months after completion of first-line platinum-based therapy. The typical patient was a 58-year-old woman with a body surface area of 1.75 m2 and serum creatinine of 0.9.

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

Dates to which data relate
The clinical and resource use data were derived from studies published between 1998 and 2006. The price year was 2006.

Modelling
A Markov model was constructed to simulate the management of disease in a hypothetical cohort of women. The time horizon of the model was 42 months with 3-month cycles. The health states considered in the model were "no evidence of disease", "no evidence of disease with neurotoxicity" and "recurrence". A graphical representation of the model was provided, together with details of possible transitions between health states.

Study designs and other criteria for inclusion in the review
The clinical data used in the model were progression-free survival (PFS), the relative risk of recurrence or death for GC and PC compared with C, and adverse events (G-CSF support, platelet transfusion, blood transfusion, neurologic grade 2-4, neurologic grade 4).

Sources searched to identify primary studies
All clinical data came from RCTs, details of which were not reported. The authors highlighted the fact that no direct comparison between GC and PC was used, thus an indirect comparison was made, using C as a common comparator.
from two different trials. Thus, the relative risk for PC and GC with respect to C was superimposed on the absolute treatment effect of each drug in their main trial.

**Methods used to derive estimates of effectiveness**
The primary studies appear to have been identified selectively as no systematic review of the literature was conducted. The data do not appear to have been combined, but each estimate was taken from a single source.

**Measure of benefits used in the economic analysis**
The summary benefit measure used was progression-free month (PFM). Results were also presented using the benefit of progression-free year (PFY). These benefits were derived using the decision model analysis. In a sensitivity analysis, quality-adjusted life-years were calculated by applying utility weights to moderate to severe neurotoxicity health states. These estimates were taken from published studies, details of which were not given.

**Direct costs**
The viewpoint of the analysis was that of the third-party payer. The categories of costs included were those related to treatment and adverse events (i.e., cycles of chemotherapy, neurology consultations, transfusions, various medications and hospitalisations). Treatment regimens included routine laboratory work. Professional fees and infusion costs were also included. In terms of adverse events, only those for which rates differed between groups were included in the analysis. The unit costs and the quantities of resources used were not presented separately. Medication costs were presented as the cost per cycle. The costs were derived from reimbursement data from the Centers for Medicare and Medicaid Services. When charges were used as proxies for costs, a specific cost-to-charge ratio of 0.6 was applied. The resource use data were based on data derived from the RCTs. Discounting was not relevant given the relatively short time horizon of the analysis. The price year was 2006. The medical care component of the Consumer Price Index was applied when previous costs were used.

**Statistical analysis of costs**
The costs and quantities were treated deterministically.

**Indirect Costs**
Productivity costs were not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
A deterministic sensitivity analysis was undertaken to address the issue of uncertainty surrounding the model results. The areas of uncertainty were survival (varied around published 95% confidence intervals), toxicity (rates and costs of adverse events), costs of chemotherapy regimens (to reflect regional variations and dose reductions), and utility weights associated with neurotoxicity.

**Estimated benefits used in the economic analysis**
The mean expected PFM were 8.01 (median 6.0) with C, 10.05 (median: 7.8) with PC and 10.52 (median 8.4) with GC.

**Cost results**
The average cost per patient was $4,018 with C, $5,982 with PC and $17,627 with GC.

**Synthesis of costs and benefits**
Incremental cost-effectiveness ratios (ICERs) were calculated in order to combine the costs and benefits of the alternative strategies.

The ICER of PC over C was $1,297 per PFM ($15,564 per PFY).

The ICER of GC over PC was $23,199 per PFM ($278,388 per PFY).
The sensitivity analysis showed that the base-case results were, in general, robust to variations in key clinical and economic inputs. In effect, the ranking of the strategies remained unaltered in several scenarios. The model results were, however, sensitive to variations in PFS. For example, when PFS of GC was assumed to be equivalent to that of PC, GC was dominated (more expensive and no more effective) by PC due to the additional costs. Also, when the relative risk of GC compared with C was set at its lower confidence limit, GC became relatively more cost-effective, with an ICER of $6,034 per additional PFM ($72,408 per additional PFY).

Quality of life adjustment did not alter the conclusions of the analysis. For example, when 5% of patients receiving PC were assumed to experience severe neurotoxicity, PC remained cost-effective in comparison with C, with an ICER of $1,604 per additional quality-adjusted PFM, while GC had an ICER of $14,722 per quality-adjusted PFM ($176,664 per PFY).

Authors' conclusions
The authors concluded that paclitaxel plus carboplatin (PC) represents a relatively cost-effective chemotherapy regimen in comparison with carboplatin alone (C) for women with recurrent platinum-sensitive ovarian cancer. Gemcitabine plus carboplatin (GC) was less cost-effective in comparison with PC in most scenarios, even when higher neurotoxicity was taken into account.

CRD COMMENTARY - Selection of comparators
The selection of the comparators reflected the choice of the chemotherapy regimens considered in the two key RCTs. Dosages were appropriately reported. The authors noted that a limitation of the analysis was the fact that sequential single-agent therapy was not incorporated in the model as a further comparator. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The clinical data were extracted from RCTs, which should have ensured a high internal validity, and the clinical estimates are therefore likely to be reliable. The issue of the indirect comparison between GC and PC was partly addressed by using a relative risk ratio with respect to a common comparator, C. However, there remains a risk of bias because of differences in patient population and the fact that additional regimens were given in the two different trials. The authors undertook an extensive sensitivity analysis to deal with this issue, and published confidence intervals were used to determine the impact of variations in clinical data on the results of the model.

Validity of estimate of measure of benefit
The benefit measure (i.e. PFS), which represents a widely used end point of chemotherapy regimens, was modelled. However, it is comparable only with similar programmes. The impact of the interventions on quality of life was investigated only in the sensitivity analysis, since the results of the RCTs supported the view that the three regimens were similar in terms of quality of life.

Validity of estimate of costs
The analysis of the costs was consistent with the stated perspective. Medicare reimbursement rates were chosen, given the viewpoint of the third-party payer. A breakdown of the cost items was not given, the costs being presented as macro-categories, reflecting the typical accounting system of third-party payers in the USA. When charges were available, a cost-to-charge ratio was appropriately applied. Statistical analyses of the costs were not performed but key cost estimates were varied in the sensitivity analysis. The authors justified the exclusion of some cost categories that were common to the three regimens. The price year was reported, which will help in reflating the results of the analysis in other time periods.

Other issues
The authors reported some results from another study that did not find combination therapy in recurrent ovarian cancer to be a cost-effective strategy. The issue of the generalisability of the study results to other settings was not explicitly addressed, although some sensitivity analyses on the costs were performed. Overall, the information underlying the analysis was satisfactorily reported and the results of the base-case analysis, as well as those of the sensitivity analysis, were clearly presented. The study referred to women requiring second-line therapy for platinum-sensitive ovarian cancer and this was reflected in the authors' conclusions.
Implications of the study
The study results provide some support for the use of PC for the treatment of recurrent platinum-sensitive ovarian cancer in comparison with both C monotherapy and GC, which were marginally less cost-effective.

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MeSH
Adult; Aged; Antineoplastic Agents /adverse effects /economics /therapeutic use; Antineoplastic Combined Chemotherapy Protocols /economics /therapeutic use; Carboplatin /administration & dosage /economics /therapeutic use; Cost-Benefit Analysis; Deoxycytidine /administration & dosage /analogs & derivatives /economics; Disease-Free Survival; Drug Costs; Female; Humans; Middle Aged; Neoplasm Recurrence, Local /drug therapy /economics; Ovarian Neoplasms /drug therapy /economics; Paclitaxel /administration & dosage /economics; Quality of Life

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