A cost-effectiveness analysis of chemotherapy for patients with recurrent platinum-sensitive epithelial 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
The study examined several strategies for the treatment of patients with recurrent platinum-sensitive advanced epithelial ovarian cancer (EOC).

Strategy 1 was best supportive care (BSC). It consisted of a multi-disciplinary approach with a team of physicians, nurses, health care aides, and social workers to address palliative care symptoms. It included paracentesis, thoracentesis and percutaneous gastrostomy tube placements, but excluded radiation therapy and chemotherapy.

Strategy 2 was second-line chemotherapy with a single drug (monotherapy). Patients received carboplatin (AUC dose of 5) every 3 weeks for six cycles.

Strategy 3 was second-line chemotherapy with two drugs (combination therapy). Patients received both carboplatin (AUC of 5) and paclitaxel (175 mg/m2) every 3 weeks for six cycles.

Strategy 4 was third-line chemotherapy after disease progression on second-line monotherapy or combination therapy. Both strategies assessed consisted of liposomal doxorubicin monthly (40 mg/m2) for six cycles.

Strategy 5 was fourth-line chemotherapy after disease progression on second- and third-line chemotherapy. This consisted of gemcitabine (1,000 mg/m2) on days 1 and 8 for four cycles. Two separate fourth-line strategies were also assessed, depending on whether second-line monotherapy or combination chemotherapy was initially used at recurrence.

Type of intervention
Palliative care and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients with recurrent platinum-sensitive EOC. All women were initially treated with primary cytoreductive surgery and combination platinum/taxane-based chemotherapy. Patients who responded with a progression-free survival (PFS) of greater than 6 months were considered platinum-sensitive.

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

Dates to which data relate
The clinical data were derived from studies published between 1998 and 2005. No dates for resource use were reported.
The price year was 2004.

**Source of effectiveness data**
The clinical data used in the study were PFS and overall survival associated with the strategies under examination.

**Modelling**
The authors stated that a decision analysis model was constructed in a hypothetical cohort of 10,000 eligible women, but no information on the model was provided. It would appear that the authors only calculated the costs and benefits through standard calculations.

**Sources searched to identify primary studies**
The clinical data were derived from Phase II and III chemotherapy studies, details of which were not given. The treatment effect of carboplatin as second-line monotherapy came from 3 studies, while 5 studies provided data on paclitaxel and carboplatin as second-line combination therapy. Three studies were used for liposomal doxorubicin as a third-line agent and for gemcitabine as a fourth-line agent. Data for BSC were obtained from a published study plus clinical experience.

**Methods used to judge relevance and validity, and for extracting data**
A review of the literature was undertaken to identify the primary studies. However, details of the review were not given.

**Measure of benefits used in the economic analysis**
The summary benefit measure was overall survival, which was derived from the literature. Discounting was not relevant given the short survival of EOC patients.

**Direct costs**
The viewpoint of the analysis was that of the third-party payer. The analysis included the costs associated with outpatient office visits, emergency department visits, hospitalisations, home health care, laboratory tests and chemotherapy cycles (chemotherapy, infusion, laboratory tests, intravenous fluids, and support medications such as antiemetics and steroids). The costs of chemotherapy-related toxicity and complications were not included. Some unit costs (especially drug costs) were given, but little information on resource use was provided. The sources of the resource use data were not reported, but standard dosages for chemotherapy regimens were used. The costs were estimated by adjusting local charges using a cost-to-charge ratio of 60%. Laboratory and procedure cost estimates were obtained from the University of Alabama at Birmingham. Pharmacy costs were calculated using average wholesale drug costs. The sources of other costs were not reported, although some might have been derived from published studies. Discounting was not performed, perhaps because of the poor survival of patients. The price year was 2004.

**Statistical analysis of costs**
The costs were treated deterministically in the base-case.

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

**Currency**
US dollars ($).
Sensitivity analysis
A univariate sensitivity analysis was carried out to assess the robustness of cost-effectiveness ratios to variations in overall survival and the costs of some strategies. Alternative values were based on authors' estimates.

Estimated benefits used in the economic analysis
The expected overall survival was:

- 6 months with BSC;
- 14 months with second-line monotherapy and 17 months with second-line combination therapy;
- 18 months with third-line previous monotherapy and 21 months with third-line previous combination therapy; and
- 21 months with fourth-line previous monotherapy and 24 months with fourth-line previous combination therapy.

Cost results
The expected costs in a hypothetical cohort of 10,000 women were:

- $244 million with BSC;
- $405 million with second-line monotherapy and $521 million with second-line combination therapy;
- $625 million with third-line previous monotherapy and $741 million with third-line previous combination therapy; and
- $1,032 million with fourth-line previous monotherapy and $1,147 million with fourth-line previous combination therapy.

Synthesis of costs and benefits
Average and incremental cost-effectiveness ratios (ACER and ICER; i.e. the average cost per month of survival and the incremental cost per life-year gained, respectively) were calculated in order to combine the costs and benefits of the alternative strategies.

The ACER was:

- $4,065 with BSC;
- $2,896 with second-line monotherapy and $3,062 with second-line combination therapy;
- $3,475 with third-line previous monotherapy and $3,527 with third-line previous combination therapy; and
- $4,914 with fourth-line previous monotherapy and $4,779 with fourth-line previous combination therapy.

The incremental analysis revealed that third- and fourth-line previous monotherapy strategies were dominated (i.e. they were less effective and more expensive than the other strategies). For the remaining strategies, the ICER was $24,228 with second-line monotherapy over BSC, $46,068 with second-line combination therapy over second-line monotherapy, $66,012 with third-line previous combination therapy over second-line combination therapy, and $162,552 with fourth-line combination therapy over third-line previous combination therapy.

The sensitivity analysis showed that the third-line previous combination therapy strategy became cost-effective (ICER < $50,000) only if overall survival exceeded 23 months (21 in the base-case). The fourth-line previous combination therapy strategy was cost-effective when overall survival exceeded 33 months (27 in the base-case). Finally, the third-line previous combination therapy strategy became cost-effective when the costs were less than $25,000.
Authors' conclusions
Second-line chemotherapy was a cost-effective strategy for patients with platinum-sensitive recurrent epithelial ovarian cancer (EOC). The choice of using a single agent versus combination therapy depended on factors such as response rates, performance status, age and history of chemotherapy-related complications. It was pointed out that third-line chemotherapy approached a reasonable cost-effectiveness value (approximately $50,000 per life-year gained) under some conditions (overall survival of 23 months or cost less than $25,000).

CRD COMMENTARY - Selection of comparators
The choice of the comparators appears to have been appropriate in that several possible strategies for patients with platinum-sensitive recurrent EOC were taken into account. The dosages used were reported in detail. Cisplatin or topotecan may also have been possible comparators for second-line strategy. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The clinical data were identified through a review of the literature, the methods and conduct of which were not reported. The authors stated that Phase II and III chemotherapy studies were considered, but details of these primary studies were not given, which limits the possibility of judging the validity of the sources of data.

Validity of estimate of measure of benefit
The summary benefit measure appears to have been derived directly from published studies. It was therefore not modelled. Discounting was not performed because of the poor survival of patients with recurrent EOC. Survival has the advantage of being comparable with the benefits of other health care interventions.

Validity of estimate of costs
The analysis of the costs was consistent with the authors’ stated perspective and the costs included were appropriate. However, there was no formal justification for the exclusion of some cost items, such as adverse events associated with chemotherapy regimens. A detailed breakdown of cost items was not given, and some costs were presented as macro-categories. In effect, only some unit costs were reported. The sources of the costs were not given in detail for all items. This reduces the possibility of replicating the analysis in other settings. Statistical analyses of the costs were not performed and only a few items were varied in the sensitivity analysis. The price year was reported, which has potential implications for the generalisability of the cost analysis in other time periods.

Other issues
The authors did not compare their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. The limited use of sensitivity analyses only partially enhances the external validity of the study. In general, the analysis of uncertainty around clinical and economic parameters appears to have been rather weak. The authors noted some limitations of their analysis such as the uncertain nature of some model inputs, the hypothetical nature of the analysis, the choice of chemotherapy agents and a non-clinical trial setting.

Implications of the study
The study results suggest that BSC and second-line chemotherapy should be recommended for the treatment of patients with platinum-sensitive recurrent EOC. The ultimate choice of the most appropriate therapy should be based on factors such as clinical aspects, patient expectations and quality of life.

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