Treatments for newly diagnosed advanced ovarian cancer: analysis of survival data and cost-effectiveness evaluation
Messori A, Trippoli S, Becaglì P, Tendi E

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
Treatments for newly diagnosed advanced ovarian cancer: (1) cisplatin-based chemotherapy at conventional doses without paclitaxel; (2) paclitaxel + cisplatin at conventional doses; and (3) high-dose chemotherapy with autologous hematopoietic rescue.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with newly diagnosed advanced ovarian cancer.

Setting
Secondary care. The economic study was carried out in Italy.

Dates to which data relate
Effectiveness data were derived from a series of trials published between 1984 and 1997. Cost estimates were derived from the literature published between 1995 and 1997.

Source of effectiveness data
The estimate of final outcomes was based on a review of previously completed studies.

Outcomes assessed in the review
Patients’ survival from the time of diagnosis, or from the beginning of the first line treatment, was the outcome assessed in the review.

Study designs and other criteria for inclusion in the review
Only large English language clinical trials, involving cases of newly diagnosed advanced ovarian cancer (with at least 50 patients per treatment modality), and which measured patients’ survival from the time of diagnosis or from the beginning of the first line treatment, were eligible for analysis.

Sources searched to identify primary studies

NHS Economic Evaluation Database (NHS EED)
Literature searches of the IOWA Drug Information System from January 1985 to September 1997, and of MEDLINE from 1 January 1980 to 30 September 1997, were carried out. Textbooks and experts in the field were also consulted, and all references in the trials retrieved were reviewed.

Criteria used to ensure the validity of primary studies
The studies included enrolled cases of newly diagnosed advanced ovarian cancer (with at least 50 patients per treatment arm) and measured the patients' survival from the time of diagnosis or from the beginning of the first-line treatment.

Methods used to judge relevance and validity, and for extracting data
The judgement criteria for assessing the validity of the primary studies were not stated. The published graphs summarising survival results from each study were used to extract data from the primary studies.

Number of primary studies included
Only 15 studies met the criteria of the review and were therefore included in the analysis.

Methods of combining primary studies
In cases where more than one trial was available evaluating a given treatment, the trial specific values of the area under the survival curve (AUC) and the mean lifetime survival (MLS) were aggregated to yield a pooled meta-analytic value. The trial specific values were weighted according to sample size.

Investigation of differences between primary studies
The authors investigated the differences between the primary studies focussing on the wide criteria for patient selection.

Results of the review
Treatment with paclitaxel+cisplatin provided no survival advantage compared with conventional cisplatin-based chemotherapy without paclitaxel. MLS values of 2.95 undiscounted years in the paclitaxel group versus 3.05 undiscounted years in the cisplatin group were reported, (p>0.05)). The patients treated with high-dose regimens and hematopoietic rescue had the longest survival (MLS=5.76 undiscounted years). In the comparison between the latter treatment versus cisplatin-based chemotherapy without paclitaxel, the survival advantage was statistically significant with MLS values of 5.76 undiscounted years in the transplantation group versus 3.05 undiscounted years in the standard cisplatin-therapy group, (p<0.05)).

Measure of benefits used in the economic analysis
Life years gained was the outcome measure used in the economic analysis. Benefits were discounted at 5%.

Direct costs
Only incremental costs reflecting the expenditure of health care resources were considered. Hospitalisation and drugs were the main components of therapy cost. Quantities and costs were not analysed separately. Cost estimates for autologous transplantation (ABMT) and peripheral blood stem cell (PBSC) rescue were derived from information published in the literature over the period from 1 January 1995 to 30 September 1997. Long-term follow-up costs were assumed to be identical across the three treatment modalities. Costs were discounted at 5%.

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

Sensitivity analysis
The first sensitivity analysis took account of the survival data from one study that reported less impressive survival data for transplanted patients. The second sensitivity analysis varied the cost of hematopoietic rescue between $20,000 to $120,000. The third sensitivity analysis utilised an annual discount rate of 3%. The fourth sensitivity analysis introduced an adjustment for quality of life.

Estimated benefits used in the economic analysis
The benefits were not presented separately.

Cost results
In the primary analysis the authors used a cost of high-dose therapy with hematopoietic rescue of $60,000 per patient. No short-term costs for paclitaxel+cisplatin therapy at conventional doses were reported.

Synthesis of costs and benefits
In the comparison between paclitaxel+cisplatin versus cisplatin-based regimens without paclitaxel, the cost-effectiveness ratio was not calculated because no survival difference was found in the analysis. In the comparison between high-dose treatments with hematopoietic rescue versus standard cisplatin-based regimens without paclitaxel, the survival gain was 2.34 (discounted) years per patient and the cost-effectiveness ratio was $25,641 (discounted) per discounted life year gained.

In the first sensitivity analysis, use of the less impressive survival data for transplanted patients resulted in a cost-effectiveness ratio of $47,619 per life year gained.

Despite the wide variations in the cost of hematopoietic rescue in the second sensitivity analysis, the cost per life year gained using high-dose treatments remained in the range of an acceptable cost-effectiveness profile (range: $8,574 to $51,282 per life year gained).

The third sensitivity analysis utilised an annual discount rate of 3% and produced a survival gain of 2.48 years per patient (MLS=5.22 years for transplantation and 2.74 years for platinum regimens) and a cost-effectiveness ratio of $24,193 per life year gained.

The fourth sensitivity analysis introduced adjustment for quality of life and compared high-dose treatments with hematopoietic rescue versus standard cisplatin-based regimens without paclitaxel. The gain was 1.88 QALYs per patient (mean lifetime value=3.54 QALYs for transplantation and 1.66 for platinum regimens) and the cost-utility ratio was $31,915 per QALY gained.

Authors’ conclusions
High-dose regimens with hematopoietic rescue can be more effective than standard chemotherapy and can substantially prolong survival at acceptable costs. The cost-utility ratio was slightly less favourable but remained within acceptable limits.

CRD COMMENTARY - Selection of comparators
The reason for the choice of comparators was clear as they were the main therapeutic options currently available for patients with newly diagnosed advanced ovarian cancer in the authors' setting. You, as a database user, should consider whether this applies to your own setting.
Validity of estimate of measure of benefit
The authors provided sufficient detail about the methodology of deriving the effectiveness evidence, although they did not explicitly define it as a systematic review of the literature. As the authors noted, the main limitation of the study was that the survival information for high-dose regimens with transplantation and paclitaxel+cisplatin was derived from one study only. They suggest that further clinical trials will be needed to confirm the results. In addition, the analysis was based on historical comparisons of clinical information derived from controlled and uncontrolled clinical studies that separately assessed patients treated with one of the three treatment options.

Validity of estimate of costs
Estimates of costs were based on the literature and did not include productivity losses of patients and costs to others in society. Resource quantities were not reported separately from prices.

Other issues
Extensive sensitivity analyses were performed to account for the uncertainties in the data. In addition, quality of life adjustments were introduced in one of the sensitivity analyses to explore their effects on the final results. Appropriate comparisons were made with other studies.

Implications of the study
According to the authors, their work suggests that high-dose regimens with hematopoietic rescue can be more effective than standard chemotherapy and can substantially prolong survival at acceptable costs. This should be further explored in well-designed RCTs allowing a head-to-head comparison of the main therapeutic options for newly diagnosed advanced ovarian cancer.

Source of funding
None stated.

Bibliographic details

PubMedID
9877236

Indexing Status
Subject indexing assigned by NLM

MeSH
Antineoplastic Combined Chemotherapy Protocols /economics /therapeutic use; Area Under Curve; Blood Component Transfusion /economics; Clinical Trials as Topic; Cost-Benefit Analysis /economics; Direct Service Costs; Female; Humans; Ovarian Neoplasms /economics /mortality /therapy; Sensitivity and Specificity; Survival Analysis

AccessionNumber
21998001201

Date bibliographic record published
31/03/2001

Date abstract record published
31/03/2001