Cost effectiveness of concurrent gemcitabine and cisplatin with radiation followed by adjuvant gemcitabine and cisplatin in patients with stages IIB to IVA carcinoma of the cervix

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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.

CRD summary
The study examined the cost-effectiveness of standard cisplatin chemoradiation versus gemcitabine plus cisplatin chemoradiation followed by two cycles of adjuvant gemcitabine and cisplatin for the management of locally advanced cervix cancer. The authors concluded that the gemcitabine regimen improved survival and provided value-for-money from the perspective of the payer. The analysis used conventional cost-effectiveness methodology that reported the key model assumptions. The authors’ conclusions rely on a randomised clinical trial results and appear to be robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The study examined the cost-effectiveness of gemcitabine plus cisplatin chemoradiation followed by two cycles of adjuvant gemcitabine and cisplatin versus standard cisplatin chemoradiation for the management of locally advanced cervix cancer (stages IIb to IVA).

Interventions
The two treatments compared were standard cisplatin chemoradiation versus the addition of gemcitabine to standard cisplatin chemoradiation.

Standard cisplatin chemotherapy consisted of cisplatin (40mg/m²) for six weeks concurrent with external-beam radiotherapy (50.4 Gy in 28 fractions) followed by low to intermediate dose rate brachytherapy (30 to 35 Gy).

Gemcitabine (235mg/m²) was given with standard cisplatin chemoradiation for six weeks, followed by two cycles of adjuvant cisplatin (50mg/m² cycle day one) and gemcitabine (1,000 mg/m² cycle day one and eight) given three weeks apart.

Location/setting
USA/hospital.

Methods
Analytical approach:
The analysis was based on a modified Markov state transition model with a time horizon of five years. The authors stated that the perspective of the payer was adopted.

Effectiveness data:
The clinical side of the analysis relied on the results of a recently published randomised controlled trial (RCT). This trial (Duenas-Gonzalez 2011, see Other Publications of Related Interest) enrolled 259 patients in the gemcitabine group (mean age 45 years) and 256 patients in the cisplatin group (mean age 46 years). This trial provided data on treatment effect and toxicity rate. The primary endpoint was the rate of overall survival.

Monetary benefit and utility valuations:
Utility valuations associated with the standard cisplatin regimen were taken from a published study; those for the
gemcitabine regimen were assumed to have been similar to those observed in the comparator group.

**Measure of benefit:**
Quality-adjusted life-years (QALYs) were used as the summary benefit measure.

**Cost data:**
The costs included were those for the interventions under examination (chemotherapy drugs, radiation, laboratory studies, and administration/infusion fees), adverse events, and those attributed to the last year of life. Costs were taken from Medicare reimbursement rates and the Healthcare Cost and Utilization Project. Costs of the last year of life came from a Dutch study. Costs were in US $. A 3% annual discount rate was applied. The price year was 2011.

**Analysis of uncertainty:**
One-way sensitivity analyses were carried out by varying probability rates and costs of toxicities, utility valuations, and transfusion rates. Clinically reasonable ranges were used.

**Results**
The expected five-year costs were $41,330 with standard cisplatin chemotherapy and $60,974 with the gemcitabine regimen. QALYs associated with the two treatments were not clearly reported.

The incremental cost per QALY gained with the gemcitabine regimen over standard cisplatin chemotherapy was $33,080.

The sensitivity analysis confirmed the robustness of the base-case analysis except for decrements in the utility values of the gemcitabine group. Specifically, for utility values decreased to 0.64, the incremental cost per QALY gained increased to $50,000 per QALY; and for utility values decreased to 0.53, the incremental cost per QALY gained was $100,000 per QALY (base case utility score was 0.76).

**Authors’ conclusions**
The authors concluded that the gemcitabine regimen improved survival and provided value-for-money from the perspective of the payer compared with the standard cisplatin chemoradiation.

**CRD commentary**
**Interventions:**
The rationale for the selection of the comparators was clear, as two the strategies under examination were the comparators in a recent clinical trial.

**Effectiveness/benefits:**
Clinical data came from a previously published head-to-head clinical trial. The randomised design of the trial and the relatively large sample of patients involved were the strengths of this trial. Study results were clearly reported but no variation in overall survival was considered in the sensitivity analysis. More information to fully judge the validity of the clinical inputs might be found in the primary publication.

QALY were appropriately used as the benefit measure because the disease affected both survival and quality of life in patients with cancer. Some assumptions were required to estimate utility valuations associated with the gemcitabine regimen, while for standard cisplatin chemotherapy were taken from a published study, whose methodological characteristics were not given. Variations in quality-of-life estimates were appropriately taken into account in the sensitivity analysis.

**Costs:**
The costs and sources used reflected the perspective of the payer. Information on unit costs and dosages for regimens compared were provided. Other costs were presented as total costs. Typical US sources were used, except for the costs of the last year of life, which was taken from a Dutch study. The price year was reported, which allowed for reflation exercises. Some cost estimates were varied in the sensitivity analysis.

**Analysis and results:**
An incremental approach was used to combine costs and benefits of the two strategies. The most cost-effectiveness option was chosen on the basis of conventional thresholds. Uncertainty was investigated by means of a deterministic analysis that considered variations in individual inputs. A more comprehensive sensitivity analysis would have been useful. The study results were selectively reported; the expected QALYs were not clearly stated. The authors acknowledged that a limitation of the study was the assumptions that costs were associated only to one hospitalisation, while multiple hospitalisations were not considered. Study findings might be specific only to the US context.

Concluding remarks:
The analysis used a conventional cost-effectiveness methodology that reported the key model assumptions. The authors’ conclusions rely on the results of a randomised clinical trial and appear robust.

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