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Title **The Clinical Effectiveness and Cost Effectiveness of Gemcitabine for Metastatic Breast Cancer: A Systematic Review and Economic Evaluation**

Agency **NCCHTA, National Coordinating Centre for Health Technology Assessment**
Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX, United Kingdom;
Tel: +44 2380 595586, Fax: +44 2380 595639

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Aim

To assess the clinical and cost effectiveness of gemcitabine used in combination with paclitaxel as second-line treatment for people with metastatic breast cancer who have relapsed following treatment with anthracycline-based chemotherapy.

Conclusions and results

The systematic review identified one RCT where data were available only in 3 conference abstracts. The methodological quality and quality of reporting of the trial were assessed to be poor, but this may be due to the lack of information in the limited publications rather than being a fair reflection of the trial's quality. This RCT compared gemcitabine and paclitaxel therapy with paclitaxel monotherapy in 529 patients with metastatic breast cancer who had previously received anthracyclines, but no prior chemotherapy for metastatic breast cancer.

Survival at 1 year was statistically significantly better in the gemcitabine/paclitaxel (G/P) group than the paclitaxel group. Approximately 71% of the G/P patients survived for 1 year, versus 61% of the paclitaxel group. The hazard ratio showed a 26% lower chance of survival in the paclitaxel group, and time to progressive disease was also shorter in this group. The overall response rate was higher in the G/P group than in the paclitaxel group. Adverse events, particularly neutropenia, were more common with G/P combination therapy than with paclitaxel therapy alone.

The economic model developed for this review was run for a simulation of 1000 patients, assuming that chemotherapy continued until patients' disease progressed. This base-case analysis found an ICER of GBP 58 876 per QALY gained and GBP 30 117 per life-year gained. In normal practice, patients are likely to receive chemotherapy for a fixed number of cycles, rather than until disease progression. Hence, the model was re-run with treatment restricted to 6 cycles (maximum) per patient, yielding an ICER of GBP 38 699 per QALY gained and GBP 20 021 per life-year gained.

Recommendations

We can draw only tentative conclusions since our review of clinical effectiveness is based on data from a single RCT, which has not yet been fully published. Evidence from the RCT may indicate that treatment with gemcitabine and paclitaxel improves outcome for patients in terms of survival and disease progression, but at the cost of increased toxicity. An economic model developed for this review reflects high costs per QALY for this treatment combination. The base-case analysis shows high ICERs, with costs per QALY gained close to GBP 60 000. Limiting chemotherapy to 6 cycles (max) gives a more favorable cost-effectiveness estimate, but still exceeds the amount usually considered as a cost-effective treatment from an NHS perspective.

Methods

The literature was systematically reviewed, and a model was developed for economic evaluation. Electronic databases were searched from inception to March 2006 and reference lists from retrieved papers were checked for further publications. Clinical advisers were asked about additional studies. Standard criteria developed by the Centre for Reviews and Dissemination were used to assess the quality of RCTs. Study reports were tabulated and synthesized in a narrative summary. A Markov state transition model was developed to estimate the cost effectiveness of gemcitabine with paclitaxel for patients with metastatic breast cancer. The model consisted of 4 states (responsive, stable disease, progressive disease, and death) and applied transition probabilities. Sensitivity analyses were carried out to estimate the effect of treating for a maximum of 6 cycles of chemotherapy.

Further research/reviews required

Further research should include an update of this review in 12 to 18 months, by which time the included RCT should be fully published. It would also be useful to compare gemcitabine with current treatments for metastatic breast cancer, including capecitabine and vinorelbine.

Written by Dr Andrea Takeda, SHTAC, United Kingdom

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