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[Intervention Review]

Antitumour antibiotic containing regimens for metastatic breast cancer

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ABSTRACT

Background

Antitumour antibiotics are used in the management of metastatic breast cancer. Some of these agents have demonstrated higher tumour response rates than non-antitumour antibiotic regimens, however a survival benefit has not been established in this setting.

Objectives

To review the randomised evidence comparing antitumour antibiotic containing chemotherapy regimens with regimens not containing an antitumour antibiotic in the management of women with metastatic breast cancer.

Search methods

The Specialised Register maintained by the Cochrane Breast Cancer Group was searched on 3rd October, 2006 using the codes for 'advanced breast cancer' and 'chemotherapy'. Details of the search strategy and coding applied by the Group to create the register are described in the Group's module on The Cochrane Library.

Selection criteria

Randomised trials comparing antitumour antibiotic containing regimens with regimens not containing antitumour antibiotics in women with metastatic breast cancer.

Data collection and analysis

Data were collected from published trials. Studies were assessed for eligibility and quality, and data were extracted by two independent reviewers. Hazard Ratios (HRs) were derived from time-to-event outcomes where possible, and a fixed effect model was used for meta-analysis. Response rates were analysed as dichotomous variables. Quality of life and toxicity data were extracted where present. A primary analysis was conducted for all trials and by class of antitumour antibiotic.

Main results

Thirty-four trials reporting on 46 treatment comparisons were identified. All trials published results for tumour response and 27 trials published time-to-event data for overall survival. The observed 4244 deaths in 5605 randomised women did not demonstrate a statistically significant difference in survival between regimens that contained antitumour antibiotics and those that did not (HR 0.96, 95% CI 0.90 to 1.02, P = 0.22) and no significant heterogeneity. Antitumour antibiotic regimens were favourably associated with time-to-progression

(HR 0.84, 95% CI 0.77 to 0.91) and tumour response rates (odds ratio (OR) 1.33, 95% CI 1.21 to 1.48) although statistically significant heterogeneity was observed for these outcomes. These associations were consistent when the analysis was restricted to the 30 trials that reported on anthracyclines. Patients receiving anthracycline containing regimens were also more likely to experience toxic events compared to patients receiving non-antitumour antibiotic regimens. No statistically significant difference was observed in any outcome between mitoxantrone containing and non-antitumour antibiotic-containing regimens.

Authors' conclusions

Compared to regimens without antitumour antibiotics, regimens that contained these agents showed a statistically significant advantage for tumour response and time to progression in women with metastatic breast cancer but were not associated with an improvement in overall survival. The favourable effect on tumour response and time to progression observed in anthracycline containing regimens was also associated with greater toxicity.

PLAIN LANGUAGE SUMMARY

Antitumour antibiotic containing regimens for metastatic breast cancer

Advanced (metastatic) breast cancer is cancer that has spread beyond the breast. Treatment for metastatic disease usually involves some type of chemotherapy (anti-cancer drugs) to try to reduce the cancer. Chemotherapy drugs can either be given as a single agent or in combination with other chemotherapy drugs. This is done according to a plan or a course of the drug referred to as a regimen. There are many types of chemotherapy drugs which work in various ways. Antitumour antibiotics work by damaging the cancer cells thereby preventing those cells from multiplying. Chemotherapy in general produces a range of side effects or adverse events related to the treatment. The known side effects of antitumour antibiotics include nausea, vomiting, a reduction in the number of white blood cells (known as leukopenia), and in some cases a toxic reaction which alters the working of the heart (called cardiotoxicity).

This review sought to identify and review the randomised evidence comparing courses of chemotherapy containing antitumour antibiotics against courses not containing antitumour antibiotics. This review identified 34 eligible trials involving 5605 women. This review found that for women with advanced breast cancer, taking antitumour antibiotics did not result in better survival than women who took other types of chemotherapy drugs. Despite the lack of evidence of survival benefit, this review demonstrated that women taking these drugs had an advantage in time to progression (the length of time it takes for the cancer to progress after taking the drug) and tumour response (shrinking of the tumour) compared to women who did not take the antitumour antibiotic drugs. In addition however, the risks of side effects including cardiotoxicity, leukopenia and nausea/vomiting were all significantly increased in the women taking the antitumour antibiotics. Given that this review failed to show a benefit in survival for women taking this group of drugs but a higher rate of side effects, the use of these drugs in the management of metastatic breast cancer must be carefully weighed against the risk of these side effects.