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Cochrane Database Syst Rev. 2002;(1):CD000487.

Multi-agent chemotherapy for early breast cancer.

Early Breast Cancer Trialists' Collaborative Group.

Update in:

Cochrane Database Syst Rev. 2008;(4):CD000487.

Abstract

BACKGROUND: There have been many randomised trials of adjuvant prolonged polychemotherapy among women with early breast cancer, and an updated overview of their results is presented.

OBJECTIVES: In this report, the Early Breast Cancer Trialists' Collaborative Group present their updated systematic overview (meta-analysis) of treatment with polychemotherapy.

SEARCH STRATEGY: Trial identification procedures for the EBCTCG overviews have been described elsewhere. See under "EBCTCG" in the Breast Cancer Collaborative Review Group module.

SELECTION CRITERIA: All randomised trials that began before 1990 and involved treatment groups that differed only with respect to the chemotherapy regimens that were being compared.

DATA COLLECTION AND ANALYSIS: In 1995, information was sought on each woman in any randomised trial that began before 1990 and involved treatment groups that differed only with respect to the chemotherapy regimens that were being compared. Analyses involved about 18,000 women in 47 trials of prolonged polychemotherapy versus no chemotherapy, about 6000 in 11 trials of longer versus shorter polychemotherapy, and about 6000 in 11 trials of anthracycline-containing regimens versus CMF (cyclophosphamide, methotrexate, and fluorouracil).

MAIN RESULTS: For recurrence, polychemotherapy produced substantial and highly significant proportional reductions both among women aged under 50 at randomisation (35% [SD 4] reduction; $2p < 0.00001$) and among those aged 50-69 (20% [SD 3] reduction; $2p < 0.00001$); few women aged 70 or over had been studied. For mortality, the reductions were also significant both among women aged under 50 (27% [SD 5] reduction; $2p < 0.00001$) and among those aged 50-69 (11% [SD 3] reduction; $2p = 0.0001$). The recurrence reductions emerged chiefly during the first 5 years of follow-up, whereas the difference in survival grew throughout the first 10 years. After standardisation for age and time since randomisation, the proportional reductions in risk were similar for women with node-negative and node-positive disease. Applying the proportional mortality reduction observed in all women aged under 50 at randomisation would typically change a 10-year survival of 71% for those with node-negative disease to 78% (an absolute benefit of 7%), and of 42% for those with node-positive disease to 53% (an absolute benefit of 11%). The smaller proportional mortality reduction observed in all women aged 50-69 at randomisation would translate into smaller absolute benefits, changing a 10-year survival of 67% for those with node-negative disease to 69% (an absolute gain of 2%) and of 46% for those with node-positive disease to 49% (an absolute gain of 3%). The age-specific benefits of polychemotherapy appeared to be largely irrespective of menopausal status at presentation, oestrogen receptor status of the primary tumour, and of whether adjuvant tamoxifen had been given. In terms of other outcomes, there was a reduction of about one-fifth ($2p = 0.05$) in contralateral breast cancer, which has already been included in the analyses of recurrence, and no apparent adverse effect on deaths from causes other than breast cancer (death rate ratio 0.89 [SD 0.09]). The directly randomised comparisons of longer versus shorter durations of polychemotherapy did not indicate any survival advantage with the use of more than about 3-6 months of polychemotherapy. By contrast, directly randomised comparisons did suggest that, compared with CMF alone, the anthracycline-containing regimens studied produced somewhat greater effects on recurrence ($2p = 0.006$) and mortality (69% vs 72% 5-year survival; log-rank $2p = 0.02$). But this comparison is one of many that could have been selected for emphasis, the 99% CI reaches zero, and the results of several of the relevant trials are not yet available.

REVIEWER'S CONCLUSIONS: Some months of adjuvant polychemotherapy (eg, with CMF or an anthracycline-containing regimen) typically produces an absolute improvement of about 7-11% in 10-year survival for women aged under 50 at presentation with early breast cancer, and of about 2-3% for those aged 50-69 (unless their prognosis is likely to be extremely good even without such treatment). Treatment decisions involve consideration not only of improvements in cancer recurrence and survival but also of adverse side-effects of treatment, and this report makes no recommendations as to who should or should not be treated.

PMID: 11869577 [PubMed - indexed for MEDLINE]

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