Review: Chemotherapy and hormonal therapy reduce recurrence and mortality at 15 years in early breast cancer

Early Breast Cancer Trialists' Collaborative Group. **Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials.** Lancet. 2005;365:1687-717.

Clinical impact ratings: GIM/FP/GP ★★★★★★☆ Oncology ★★★★★★☆

QUESTION

What are the effects of adjuvant chemotherapy, tamoxifen, and ovarian ablation or suppression on recurrence and survival 15 years after diagnosis of early breast cancer?

METHODS

Data sources: MEDLINE, published lists of randomized trials, hand-searching selected journals, meeting abstracts, references of published trials and reviews, and contacting experts repeatedly over a 15-year period.

Study selection and assessment: Unconfounded randomized controlled trials (RCTs) of adjuvant systemic therapies for early breast cancer begun before 1995. Individual patient data and updated follow-up were sought on every woman included in the studies. Analyses were by intention to treat.

Outcomes: Main outcomes were death from breast cancer, death from other causes, breast cancer recurrence, and incidence of second cases of cancer.

MAIN RESULTS

194 RCTs (n = 144 939) were included and comprise about 91% of all women randomized in such trials before 2000. Standard polychemotherapy, including an anthracycline for 4 to 6 months (e.g., fluorouracil, cyclophosphamide, and either doxorubicin [adriamycin], or epirubicin [FAC or FEC]), reduced annual breast cancer mortality rates by 38% in women < 50 years of age and by 20% in women 50 to 69 years of age, and was more effective than cyclophosphamide, methotrexate, and fluorouracil (CMF) (P < 0.001). These effects were independent of axillary lymph node involvement, estrogen-receptor (ER) status, and treatment with tamoxifen. The absolute benefit of adjuvant chemo-therapy at 15 years was more than double its benefit at 5 years in women < 50 years of age (Table). Tamoxifen for 5 years in women with ER-positive disease reduced the annual breast cancer mortality rate by 31% and was more effective than tamoxifen for 1 or 2 years (P < 0.001). These effects were independent of age, menopausal status, lymph node involvement, and tumor size. The absolute benefit of tamoxifen at 15 years was more than double its benefit at 5 years (Table). Tamoxifen was ineffective in women with ER-negative disease. Ovarian ablation or suppression reduced the annual breast cancer mortality rate by 29% in the absence of chemotherapy. Deaths from causes other than breast cancer were not affected by any of the 3 treatments.

CONCLUSION

Adjuvant chemotherapy, tamoxifen, and ovarian ablation or suppression substantially reduce mortality rates over 15 years in women with early breast cancer.

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For correspondence: Early Breast Cancer Trialists' Collaborative Group Secretariat, CTSU, Radcliffe Infirmary, Oxford, England, UK. E-mail bc.overview@ctsu.ox.ac.uk.

Chemotherapy and tamoxifen for breast cancer at 15 years*

Treatment	Patient group	Annual rate ratio for breast cancer mortality over 15 y	Absolute improvement in breast cancer mortality			*P* value
			5 y	10 y	15 y	
Polychemotherapy for 4 to 6 mo including an anthracycline	Women < 50 y	0.62	4.7%	7.9%	10%	< 0.001
	Women 50 to 60 y	0.80	2.6%	2.9%	3.0%	< 0.001
Tamoxifen for 5 y	Women with ER-positive disease (any age)	0.69	3.6%	7.9%	9.2%	< 0.001

*ER = estrogen-receptor.

COMMENTARY

The EBCTCG update of previous work shows that the survival benefits of adjuvant therapy persist over time—the effect of killing or suppressing micrometastases lasts far beyond the end of treatment. In this case, the absolute benefit can be as high as 10 additional women alive per 100 treated, with no additional deaths from treatment-related diseases.

These are the minimal effects of adjuvant therapy, too, because current treatments are more effective and less toxic. Recent large RCTs show that the addition of paclitaxel to 4 cycles of doxorubicin-cyclophosphamide adds another 2 to 3 survivors per 100 women (1). We can add 2 to 3 more survivors by giving the same chemotherapy every 2 weeks instead of every 3 weeks (2). The addition of trastuzumab (Herceptin) for women whose cancer overexpresses human epidermal growth factor receptor-2 may provide even more benefit, based on its substantial effects on disease-free survival (3). A low-fat diet (about 30 g/d) may reduce relative recurrence risk a further 24% when added to these "best" therapies (4). Aromatase inhibitors improve disease-free survival more than tamoxifen alone, or when given after tamoxifen, and will probably improve overall survival (5).

How does one keep up with these developments? Adjuvant! (www.adjuvantonline.com) is a simple prediction tool to estimate the absolute benefits for women considering these treatments.

Thomas J. Smith, MD
James Khatcheressian, MD
Virginia Commonwealth University
Richmond, Virginia, USA

References

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