

Adjuvant Systemic Therapy for Node-negative Breast Cancer Practice Guideline Report #1-8

Members of the Breast Cancer Disease Site Group

ORIGINAL GUIDELINE: November 12, 1998
NEW EVIDENCE ADDED TO GUIDELINE REPORT: February 2002
MOST RECENT LITERATURE SEARCH: May 1, 2003

The Breast Cancer Disease Site Group is rewriting this practice guideline report. The revised guideline report will incorporate all new evidence that has become available since the guideline was completed in 1998. The new evidence under review is identified in the update sections of the full report below. The current guideline recommendations remain in effect until the Breast Cancer Disease Site Group has completed their review of the new evidence.

SUMMARY

Guideline Question

What is the role of systemic adjuvant therapy for women with node-negative breast cancer?

Target Population

These recommendations apply to adult patients with node-negative breast cancer.

Recommendations

Choice of Therapy

- **Pre- and postmenopausal women at minimal or low risk of recurrence** (<2 cm, well-differentiated and all other factors favourable or <1 cm, intermediate grade and all other factors favourable) should receive no adjuvant systemic treatment. They should, however, be made aware that systemic therapy is offered to women at higher risk of recurrence.
- **Premenopausal women** (age <50 years) **at moderate risk of recurrence** (1-3 cm and intermediate grade or 2-3 cm and well-differentiated) and with estrogen-receptor-positive tumours should be offered tamoxifen. Chemotherapy added to tamoxifen may provide a modest incremental benefit over tamoxifen alone. This is an ideal situation for a decision aid.
- **Premenopausal women** (age <50 years) **at high risk of recurrence** (>3 cm, irrespective of any other factors, or >1 cm with either estrogen-receptor-negative, high grade or lymphatic/vascular invasion) should be offered chemotherapy. There are insufficient data at the present time to recommend the addition of tamoxifen to chemotherapy in this subgroup. If the patient refuses chemotherapy and the tumour is estrogen-receptor-positive, tamoxifen may be considered. There is insufficient data to determine the risk category of a tumour <1 cm in diameter associated with a poor prognostic factor (e.g., grade III, estrogen-receptor-negative, lymphatic/vascular invasion).

- **Postmenopausal women** (age >50 years) **at high risk of recurrence** (>3 cm, or >1 cm with high grade or lymphatic/vascular invasion) and with estrogen-receptor-positive tumours should be offered tamoxifen plus chemotherapy. The benefits and risks of additional chemotherapy should be discussed with the patient. If the patient refuses chemotherapy, then tamoxifen alone should be considered. Postmenopausal women at high risk of recurrence and with estrogen-receptor-negative tumours should be offered chemotherapy.
- **Postmenopausal women** (age >50 years) **at moderate risk of recurrence** (1-3 cm and intermediate grade or 2-3 cm and well-differentiated) and with estrogen-receptor-positive tumours should be offered tamoxifen. Chemotherapy added to tamoxifen may provide a modest incremental benefit over tamoxifen alone. This is an ideal situation for the use of a decision aid.

Duration of Tamoxifen

Hormonal therapy should consist of oral tamoxifen 20 mg daily for five years.

Chemotherapy Regimen

Polychemotherapy should reasonably comprise six cycles of cyclophosphamide (oral)/methotrexate/fluorouracil or four cycles of doxorubicin/cyclophosphamide.

Process of Decision Making

A patient with node-negative breast cancer should be informed of the availability of adjuvant systemic therapy and should be offered the opportunity of discussing such therapy with an expert clinician. She should be provided with detailed information concerning her risk of recurrence if untreated, the potential efficacy of adjuvant therapy in terms of recurrence and mortality and the potential side effects of therapy.

Methods

Entries to MEDLINE (1980-April 2003), the Cochrane Library (Issue 1, 2003) and abstracts published in the proceedings of the annual meetings of the American Society of Clinical Oncology were searched for evidence relevant to this practice guideline report.

Evidence was selected and reviewed by members of the Practice Guideline Initiative's Breast Cancer Disease Site Group. This practice guideline has been reviewed and approved by the Breast Cancer Disease Site Group, which is comprised of surgeons, medical oncologists, epidemiologists, a pathologist, a medical sociologist, and a community representative.

External review of the original practice guideline report by Ontario practitioners was obtained through a mailed survey. Final approval of the original guideline was obtained from the Practice Guidelines Coordinating Committee.

The Practice Guidelines Initiative has a formal standardized process to ensure the currency of each guideline report. This consists of the periodic review and evaluation of the scientific literature, and where appropriate, integration of this literature with the original guideline information.

Key Evidence

- Two individual-patient-data meta-analyses were updated in August 2001. One analyzed data from 17,723 women involved in 47 randomized trials of long-term polychemotherapy versus no chemotherapy. The other was based on data from 55 randomized trials of tamoxifen versus no tamoxifen with a total of 37,099 participants.
- Adjuvant chemotherapy reduced the rate of disease recurrence (24% relative reduction in the annual hazard of recurrence compared with no chemotherapy) and improved survival (relative reduction in the annual hazard of death was 15%) in women with breast cancer. Relative

reductions in recurrence and death rates were similar for patients with node-negative and node-positive disease.

- Adjuvant tamoxifen reduced the rate of disease recurrence (26% relative reduction in the annual hazard of recurrence compared with no tamoxifen) and improved survival (relative reduction in the annual odds of death was 15%) in women with breast cancer. Relative reductions in recurrence and death rates were similar for patients with node-negative and node-positive disease but did vary by length of tamoxifen treatment. Relative reductions in recurrence rates were 18% with one year of tamoxifen, 25% with two years, and 42% with five years; relative reductions in death rates were 10% with one year of tamoxifen, 15% with two years, and 22% with five years.
- Chemotherapy can be associated with a variety of adverse effects such as alopecia, nausea and vomiting, and infection. There are relatively few adverse effects associated with tamoxifen, but very rarely tamoxifen can cause venous thromboembolism or endometrial cancer.

For further information about this practice guideline report, please contact:

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PREAMBLE: About Our Practice Guideline Reports

The Practice Guidelines Initiative (PGI) is a project supported by Cancer Care Ontario (CCO) and the Ontario Ministry of Health and Long-Term Care, as part of the Program in Evidence-based Care. The purpose of the Program is to improve outcomes for cancer patients, to assist practitioners to apply the best available research evidence to clinical decisions, and to promote responsible use of health care resources. The core activity of the Program is the development of practice guidelines by multidisciplinary Disease Site Groups of the PGI using the methodology of the Practice Guidelines Development Cycle.¹ The resulting practice guideline reports are convenient and up-to-date sources of the best available evidence on clinical topics, developed through systematic reviews, evidence synthesis and input from a broad community of practitioners. They are intended to promote evidence-based practice.

This practice guideline report has been formally approved by the Practice Guidelines Coordinating Committee (PGCC), whose membership includes oncologists, other health providers, community representatives and Cancer Care Ontario executives. Formal approval of a practice guideline by the Coordinating Committee does not necessarily mean that the practice guideline has been adopted as a practice policy of CCO. The decision to adopt a practice guideline as a practice policy rests with each regional cancer network that is expected to consult with relevant stakeholders, including CCO.

Reference:

¹ Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. *J Clin Oncol* 1995;13(2):502-12.

For the most current versions of the guideline reports and information about the PGI and the Program, please visit our Internet site at:
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