



## Complete Summary

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### GUIDELINE TITLE

Adjuvant taxane therapy for women with early-stage, invasive breast cancer.

### BIBLIOGRAPHIC SOURCE(S)

Trudeau M, Eisen A, Messersmith H, Sinclair S, Pritchard K, Breast Cancer Disease Site Group. Adjuvant taxane therapy for women with early-stage, invasive breast cancer. Toronto (ON): Cancer Care Ontario (CCO); 2006 Jan 16. 29 p. (Practice guideline report; no. 1-7). [24 references]

### GUIDELINE STATUS

This is the current release of the guideline.

The EVIDENCE-BASED SERIES, initially the full original Guideline, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the [Cancer Care Ontario Web site](#) for details on any new evidence that has emerged and implications to the guidelines.

## COMPLETE SUMMARY CONTENT

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## SCOPE

### DISEASE/CONDITION(S)

Early-stage, invasive breast cancer

### GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness  
Treatment

**CLINICAL SPECIALTY**

Oncology  
Radiation Oncology

**INTENDED USERS**

Physicians

**GUIDELINE OBJECTIVE(S)**

In women with T 1-3, operable, node-positive breast cancer:

- To evaluate if a concurrent taxane-anthracycline regimen compared with a standard anthracycline-based regimen (e.g., doxorubicin and cyclophosphamide [AC], 5-fluorouracil, doxorubicin, and cyclophosphamide [FAC], 5- fluorouracil, epirubicin, and cyclophosphamide [500/100/500mg/m<sup>2</sup>] [FEC-100], or cyclophosphamide, epirubicin, 5-fluorouracil [75/60/100mg/m<sup>2</sup>] [CEF]), improves clinically meaningful outcomes (disease-free and overall survival)
- To evaluate if a sequential taxane–anthracycline regimen compared with an anthracycline-based regimen, improves clinically meaningful outcomes
- To evaluate if a dose-dense (two-weekly) regimen compared with a standard (three-weekly) anthracycline-taxane regimen, improves clinically meaningful outcomes
- To evaluate if a non-anthracycline taxane regimen compared with an anthracycline-based regimen, improves clinically meaningful outcomes
- To determine the harms associated with adjuvant taxane regimens

**TARGET POPULATION**

Women with T 1-3, operable, node-positive breast cancer

**INTERVENTIONS AND PRACTICES CONSIDERED**

1. Concurrent taxane-anthracycline regimen
2. Standard anthracycline-based regimen (e.g., doxorubicin and cyclophosphamide [AC], 5-fluorouracil, doxorubicin, and cyclophosphamide [FAC], 5- fluorouracil, epirubicin, and cyclophosphamide [FEC-100], or cyclophosphamide, epirubicin, 5-fluorouracil [CEF])
3. Sequential taxane-anthracycline regimen
4. Standard (three-weekly) anthracycline-taxane regimen
5. Dose-density (two-weekly) anthracycline-taxane regimen
6. Non-anthracycline taxane regimen

**MAJOR OUTCOMES CONSIDERED**

- Disease-free survival

- Overall survival
- Toxicity

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)  
 Hand-searches of Published Literature (Secondary Sources)  
 Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

MEDLINE (1966 to September 2004), EMBASE (1980 to September 2004), and the Cochrane Library (Issue 3, 2004) databases were searched. The MEDLINE and EMBASE search strategies are described below. The American Society of Clinical Oncology (ASCO) (1995 to 2004) and the San Antonio Breast Cancer Symposium (SABCS) (2001 to 2003) online conference proceedings were searched for reports of new or ongoing trials. Relevant articles and abstracts were selected and reviewed by three reviewers, and the reference lists from those sources were searched for additional trials, as were the reference lists from relevant review articles.

### MEDLINE and EMBASE search strategies according to disease, treatment, and study design terms.

#### Term Type

1. Disease
  - MEDLINE search strategy: Breast neoplasms (medical subject heading [MeSH])
  - EMBASE search strategy: Breast cancer (drug therapy [dt])
2. Treatment
  - MEDLINE search strategy: Taxanes [MeSH] AND antineoplastic combined chemotherapy protocols [MeSH]
  - EMBASE search strategy: Terpenoid (explode [exp]/drug combination [cb], drug comparison [cm], drug therapy) AND cancer combination therapy
3. Study design
  - MEDLINE search strategy: Meta-analysis (publication type [pt]) OR randomized controlled trial [pt]
  - EMBASE search strategy: Meta-analysis OR randomized controlled trial

#### Inclusion Criteria

Articles were eligible for inclusion in this systematic review of the evidence if they met the following criteria:

- An adjuvant taxane regimen was evaluated in a phase III randomized controlled trial. Meta-analyses of phase III randomized controlled trials were also eligible.

- Reported outcomes included disease-free survival (DFS), overall survival (OS), or toxicity.
- Clinical trial results were reported in either full papers or abstracts. Although data presented in meeting abstracts may not be as reliable and complete as that from papers published in peer-reviewed journals, abstracts can be a source of important evidence from randomized trials and add to the evidence available from fully published studies. Those data often appear first in meeting abstracts and may not be published for several years.

### **Exclusion Criteria**

Articles published in a language other than English were excluded.

### **NUMBER OF SOURCE DOCUMENTS**

Nine randomized controlled trials, described in 15 reports were eligible for inclusion in the systematic review of the evidence.

### **METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE**

Expert Consensus (Committee)

### **RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE**

Not applicable

### **METHODS USED TO ANALYZE THE EVIDENCE**

Meta-Analysis of Randomized Controlled Trials  
Systematic Review with Evidence Tables

### **DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

#### **Synthesizing the Evidence**

When clinically homogenous results from two or more trials were available, the data was pooled using the Review Manager software (RevMan 4.1) provided by the Cochrane Collaboration (Metaview © Update Software). Since hazard ratios (HR), rather than the number of events at a certain time point, are the preferred statistic for pooling time-to-event outcomes, those were extracted directly from the most recently reported trial results. The variances of the HR estimates were calculated from the reported confidence intervals (CI) using the methods described by Parmar et al. A random effects model was used for all pooling.

Statistical heterogeneity was calculated using the Chi square test for heterogeneity and the  $I^2$  percentage. A probability level for the Chi square statistic less than or equal to 10% ( $p \leq 0.10$ ) and/or an  $I^2$  greater than 50% were considered indicative of statistical heterogeneity. Results are expressed as hazard ratios with 95% CI. An HR >1.0 indicates that patients receiving a taxane had a higher probability of experiencing the presence of disease or death (DFS) or death

(OS); conversely, an HR <1.0 suggests that patients receiving a taxane experienced a lower probability of an event.

## **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

## **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

This practice guideline report was developed by the Cancer Care Ontario Program in Evidence-based Care (PEBC), using the methods of the Practice Guidelines Development Cycle. Evidence was selected and reviewed by three medical oncologist members and one methodologist member of the PEBC's Breast Cancer Disease Site Group (DSG).

The practice guideline report is a convenient and up-to-date source of the best available evidence on taxanes in the adjuvant treatment of women with early-stage invasive breast cancer developed through systematic reviews and evidence synthesis. The body of evidence in this report is primarily comprised of randomized controlled trial data; therefore, recommendations by the Breast Cancer DSG are offered.

## **RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

Not applicable

## **COST ANALYSIS**

A formal cost analysis was not performed and published cost analyses were not reviewed.

## **METHOD OF GUIDELINE VALIDATION**

External Peer Review  
Internal Peer Review

## **DESCRIPTION OF METHOD OF GUIDELINE VALIDATION**

### **Practitioner Feedback**

Practitioner feedback was obtained through a mailed survey of 109 practitioners in Ontario (77 medical oncologists and 32 radiation and/or surgical oncologists). The survey consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations above should be approved as a practice guideline. Written comments were invited. The practitioner feedback survey was mailed out on June 21, 2005. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The Breast Cancer Disease Site Group (DSG) reviewed the results of the survey.

## **Review by Report Approval Panel**

Overall, the Panel agreed this was comprehensive document that covered complex literature. Two key issues were identified by both reviewers:

- Given the range of treatment options identified, the reviewers felt that it would be helpful if the group could put the recommended options in context, for example, through use of an algorithm or examination of trade-offs between recommended treatments. However, the reviewers also acknowledged that evidence to provide such context may not be available.
- The reviewers suggested that the group consider conducting broader meta-analyses (e.g., class-specific comparisons or meta-analyses to explore potential sub-group effects).

With regard to the suggestion about meta-analyses, the Breast Cancer DSG felt that, at this time, a broader analysis would not provide significant new information with which to make broader recommendations.

## **Final Review by the Breast Cancer DSG**

During the final review process by the Breast Cancer DSG, several members raised concerns similar to those raised by the Report Approval Panel (RAP) regarding the array of treatment options. These members felt strongly that some overall statement regarding adjuvant chemotherapy was necessary to make the recommendations useful to clinicians.

## **Response to Review by the Breast Cancer DSG and the Report Approval Panel**

In response to this feedback from the Breast Cancer DSG and the Report Approval Panel, a summary recommendation was added that presented overall guidance regarding taxanes in adjuvant chemotherapy. A new meta-analysis was not conducted, as the authors felt that it would not provide sufficient additional evidence to warrant new recommendations. The Breast Cancer DSG also recognized the need for a future practice guideline that would combine all the current recommendations for adjuvant systemic therapy and provide guidance to clinicians in selecting appropriate regimens.

# **RECOMMENDATIONS**

## **MAJOR RECOMMENDATIONS**

### **Summary Recommendation**

The following taxane containing regimens are considered reasonable treatment options for the target population:

- Six cycles of three-weekly docetaxel, doxorubicin, and cyclophosphamide (TAC) (75/50/500mg/m<sup>2</sup>)
- Four cycles of doxorubicin and cyclophosphamide (AC) (60/600mg/m<sup>2</sup>) followed by four cycles of paclitaxel (175mg/m<sup>2</sup> or 225mg/m<sup>2</sup> every three

- weeks or 175 mg/m<sup>2</sup> every two weeks with granulocyte colony-stimulating factor [G-CSF]).
- Three cycles of 5-fluorouracil, epirubicin, and cyclophosphamide (FEC)-100 followed by three cycles of docetaxel (100 mg/m<sup>2</sup>)

These regimens are recommended over their non-taxane containing counterparts (six cycles of 5-fluorouracil, doxorubicin, and cyclophosphamide (FAC), four cycles of AC, and six cycles of FEC-100), as they have been shown to be superior in efficacy. Taxane-containing counterparts to other commonly used non-taxane anthracycline regimens (e.g., cyclophosphamide, epirubicin, 5-fluorouracil [CEF]) have not yet been evaluated by randomized clinical trials. However, these non-taxane-containing regimens remain reasonable treatment options.

**Question #1: Compared with a Standard Anthracycline-Based Regimen, Does a Concurrent Taxane-Anthracycline Regimen Improve Clinically Meaningful Outcomes?**

- Women in the target population are recommended to receive six cycles of three-weekly docetaxel, doxorubicin, and cyclophosphamide over six-cycles of three-weekly 5-fluorouracil, doxorubicin, and cyclophosphamide (500/50/500mg/m<sup>2</sup>).

**Question #2: Compared with an Anthracycline-Based Regimen, Does a Sequential Taxane-Anthracycline Regimen Improve Clinically Meaningful Outcomes?**

- For women in the target population, four cycles of three-weekly AC (60/600mg/m<sup>2</sup>) followed by four cycles of three-weekly paclitaxel (175mg/m<sup>2</sup> or 225mg/m<sup>2</sup>) is recommended over four cycles of three-weekly AC alone (60/600mg/m<sup>2</sup>).
- For women in the target population, three cycles of FEC-100 followed by three cycles of docetaxel (100 mg/m<sup>2</sup>) is recommended over six cycles of FEC-100 alone.

**Question #3: Compared with a Standard (Three-Weekly) Anthracycline-Taxane Regimen, Does a Dose-Dense (Two-Weekly) Regimen Improve Clinically Meaningful Outcomes?**

- Women in the target population should be considered for dose-dense therapy. In practice, four cycles of two-weekly AC (60/600mg/m<sup>2</sup>) followed by four cycles of two-weekly paclitaxel (175mg/m<sup>2</sup>) (AC followed by docetaxel [T]) is more commonly used due to a shorter duration of treatment.
- Granulocyte colony-stimulating factor (days three to 10 of each cycle [a total of seven doses] at 5 micrograms /kg rounded to either 300 micrograms or 480 micrograms total dose) should be given in combination with four cycles of two-weekly AC followed by docetaxel to prevent neutropenia.

**Question #4: Compared with an Anthracycline-Based Regimen, Does a Non-Anthracycline Taxane Regimen Improve Clinically Meaningful Outcomes?**

- There is insufficient evidence at this time to make any evidence-based recommendations regarding non-anthracycline taxane regimens versus anthracycline-based regimens.

### **Question #5: What are the Harms Associated with Adjuvant Taxane Regimens?**

- Women receiving an adjuvant anthracycline-taxane regimen should be closely monitored for febrile neutropenia. In those who experience febrile neutropenia while receiving TAC, granulocyte colony-stimulating factor (days three to ten of each cycle [a total of seven doses] at 5 micrograms/kg rounded to either 300 micrograms or 480 micrograms total dose) should be administered with subsequent docetaxel infusions. Alternatively, a dose reduction should be considered.
- Women receiving an anthracycline-taxane regimen should also be monitored for other toxicities, including diarrhea, stomatitis, amenorrhea, asthenia, myalgia, paresthesia, and leukopenia.
- Women receiving docetaxel and cyclophosphamide (TC) should be monitored for paresthesia, edema, weight gain, rash, and arthralgia.

### **CLINICAL ALGORITHM(S)**

None provided

## **EVIDENCE SUPPORTING THE RECOMMENDATIONS**

### **TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS**

The recommendations are supported by randomized controlled trials.

## **BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS**

### **POTENTIAL BENEFITS**

- In the analysis of the Breast Cancer International Research Group (BCIRG) 001 trial, (n=1,491) women receiving six cycles of three-weekly docetaxel, doxorubicin, and cyclophosphamide (TAC) (75/50/500mg/m<sup>2</sup>) experienced improved disease-free survival (DFS) (hazard ratio [HR], 0.72; 95% confidence interval [CI], 0.59 to 0.88; p<0.001) and overall survival (OS) (HR, 0.70; 95% CI, 0.53-0.91; p=0.0080) at a median follow-up of 55 months compared with women receiving six cycles of three-weekly 5-fluorouracil, doxorubicin, and cyclophosphamide (FAC) (500/50/500mg/m<sup>2</sup>).
- At median follow-ups of 69 and approximately 65 months, DFS was improved in both the Cancer and Leukemia Group B (CALGB) 9344 (n=3,121) (absolute difference, 5%; p=0.013) and National Surgical Adjuvant Breast and Bowel Project (NSABP) B-28 (n=3,060) (absolute difference, 4%; p=0.006) trials with the addition of four cycles of three-weekly paclitaxel (175mg/m<sup>2</sup> or 225mg/m<sup>2</sup>) following doxorubicin and cyclophosphamide (AC) (60-90/600mg/m<sup>2</sup>). The CALGB 9344 trial detected improved OS (absolute difference, 3%; p=0.0061) with the addition of paclitaxel whereas the NSABP

- B-28 trial did not (absolute difference, 0%;  $p=0.46$ ). The pooled OS effect estimate was statistically significant ( $p=0.02$ ). In unplanned subgroup analyses of the CALGB 9344 trial, the DFS benefit was most pronounced among women whose tumours were hormone receptor-negative, whereas in the NSABP B-28 trial, the opposite was true. The pooled DFS effect estimates were statistically significant in both the hormone receptor-positive ( $p=0.04$ ) and negative ( $p=0.04$ ) subgroups.
- In the M.D. Anderson Cancer Center (MDACC) trial ( $n=524$ ) there was a trend towards improved DFS (absolute difference, 3%;  $p=0.09$ ) with four cycles of paclitaxel followed by four cycles of FAC versus eight cycles of FAC at a median follow-up of 60 months. Overall survival was not reported.
  - In the Programmes d'Actions Concertées Sein (PACS) 01 trial ( $n=1999$ ), after a planned median follow-up of 60 months, five-year DFS was improved with a three-cycle 5-fluorouracil, epirubicin, and cyclophosphamide (FEC)-100, three-cycle docetaxel regimen as opposed to a six-cycle FEC-100 regimen (absolute difference 5.1%;  $p=0.014$ ).
  - In the Intergroup (INT)/CALGB 9741 trial ( $n=2,005$ ), four-year DFS (absolute difference, 7%;  $p=0.010$ ) and three-year OS (absolute difference, 2%;  $p=0.013$ ) were improved in women who received granulocyte colony-stimulating factor (G-CSF) and four cycles of two-weekly doxorubicin (A) followed by docetaxel (T) followed by cyclophosphamide (C) or AC followed by T compared with women who received the same regimens every three weeks at a median follow-up of 36 months
  - In the US Oncology (USON) 9735 trial ( $n=1,016$ ), there was no significant difference in DFS (absolute difference 3%;  $p=0.131$ ) or OS (absolute difference 1.5%,  $p=0.465$ ) in women randomized to receive four cycles of three-weekly docetaxel and cyclophosphamide (TC) ( $75/600\text{mg}/\text{m}^2$ ) versus AC ( $60/600\text{mg}/\text{m}^2$ ) at a median follow-up of 36 months.

## POTENTIAL HARMS

Five trials reported arm-to-arm hematologic toxicity comparisons.

- In the Breast Cancer International Research Group (BCIRG) 001 trial ( $n=1,491$ ), rates of neutropenia (66% vs. 49%,  $p\leq 0.05$ ) and febrile neutropenia (25% vs. 3%,  $p\leq 0.05$ ) were more common in women receiving docetaxel, doxorubicin, and cyclophosphamide (TAC) compared with those receiving six cycles of 5-fluorouracil, doxorubicin, and cyclophosphamide (FAC).
- In the M.D. Anderson Cancer Center (MDACC) trial ( $n=524$ ), neutropenia (44% vs. 24%;  $p$ -value not reported) and febrile neutropenia (17% vs. 9%;  $p$ -value not reported) appeared to be more common in women receiving four cycles of paclitaxel followed by four cycles of FAC compared with women receiving eight cycles of FAC alone. Granulocyte colony-stimulating factor (G-CSF) was used to treat febrile neutropenia in that trial.
- In the Grupo Español de Investigación del Cáncer de Mama (GEICAM) 9906 trial ( $n=1,249$ ), women receiving four cycles of 5-fluorouracil, epirubicin, and cyclophosphamide (FEC)-90 followed by eight cycles of weekly paclitaxel experienced more neutropenia (30% vs. 21%;  $p\leq 0.05$ ) and febrile neutropenia (9% vs. 5%,  $p=0.004$ ) compared with women in the six-cycle FEC arm.

- In the Programmes d'Actions Concertées Sein (PACS) 01 trial, after a planned median follow-up of 60 months, women receiving three cycles of FEC-100 followed by three cycles of docetaxel, compared to those receiving six cycles of FEC-100, experienced significantly less neutropenia in cycles four to six (10.9% vs. 20.2%,  $p < 0.001$ ) but significantly more febrile neutropenia regardless of cycle (4.6% vs. 1%,  $p = 0.001$ ).
- In the Intergroup Cancer and Leukemia Group B (INT/CALGB) 9741 trial ( $n = 2,005$ ), granulocyte colony-stimulating factor (G-CSF) was administered prophylactically in the dose-dense arms. Neutropenia was less frequent in the two-weekly doxorubicin (A) followed by paclitaxel followed by cyclophosphamide (C) and doxorubicin and cyclophosphamide (AC) followed by paclitaxel arms than in the three-weekly A followed by paclitaxel followed by C and AC followed by paclitaxel arms (6% vs. 33%;  $p < 0.001$ ).
- Of note, women in the CALGB 9344 and National Surgical Adjuvant Breast and Bowel Project (NSABP) B-28 trials received G-CSF to treat febrile neutropenia and as an ongoing secondary prophylaxis.
- In the BCIRG 001 trial, women receiving TAC experienced slightly higher rates of grade 3/4 diarrhea (4% vs. 2%;  $p \leq 0.05$ ), stomatitis (7% vs. 2%;  $p \leq 0.05$ ), and asthenia (11% vs. 6%;  $p \leq 0.05$ ) than those receiving FAC. In the MDACC trial, grade 3/4 myalgia (33% vs. 4%) and paresthesia (15% vs. 2%) appeared to be more common in women receiving four cycles of paclitaxel followed by four cycles of FAC compared with women receiving eight cycles of FAC alone. In the GEICAM 9906 trial, women in the paclitaxel group experienced more grade 3/4 mucositis (5% vs. 3%;  $p \leq 0.05$ ) and leukopenia (11% vs. 7%;  $p \leq 0.05$ ) compared with women in the six-cycle FEC arm. In the PACS 01 trial, patients receiving FEC followed by docetaxel experienced significantly more grade 3/4 edema (4.8% vs. 0.3%) and nail disorders (10.3% vs. 1.0%), but significantly less grade 3/4 neutropenia in cycles 4-6 (10.9% vs. 20.2%), nausea-vomiting in cycles 1 to 3 (10.1% vs. 13.2%), nausea and vomiting in cycles 4 to 6 (1.6% vs. 11.0%), and cardiac toxicity (0.4% vs. 1.3%).
- In the US Oncology (USON) 9735 trial ( $n = 1,016$ ), docetaxel-related side effects, such as paresthesia, edema, weight gain, rash, and arthralgia were more common with docetaxel and cyclophosphamide (TC), whereas more anemia, vomiting, and stomatitis were associated with AC. Grade 3 and 4 leukopenia, infections, asthenia, and hair loss were similar.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

#### **Question #1: Compared with a Standard Anthracycline-Based Regimen, does a Concurrent Taxane-Anthracycline Regimen Improve Clinically Meaningful Outcomes?**

- There are no data comparing epirubicin-based regimens such as 5-fluorouracil, epirubicin, and cyclophosphamide (FEC)-100 or cyclophosphamide, epirubicin, 5-fluorouracil (CEF) to their epirubicin- and taxane-containing counterparts. There is also no evidence directly comparing 1) doxorubicin, cyclophosphamide, and a taxane to FEC-100 or CEF or 2) 5-fluorouracil, doxorubicin, and cyclophosphamide (FAC) to FEC-100 or CEF. Therefore, there are no grounds on which to base a recommendation as to

which of FEC-100, CEF, or docetaxel, doxorubicin, and cyclophosphamide (TAC) may be preferable. However, in the case of FEC-100, see the "Major Recommendations" field.

**Question #2: Compared with an Anthracycline-Based Regimen, Does a Sequential Taxane-Anthracycline Regimen Improve Clinically Meaningful Outcomes?**

- For women in the target population, four cycles of three-weekly paclitaxel (250mg/m<sup>2</sup>) followed by four cycles of three- to four-weekly FAC (500/50/500mg/m<sup>2</sup>) (taxane [T] followed by FAC) may not be different from eight cycles of three- to four-weekly FAC; however, data are only available from one small randomized trial (n=524) for which only disease-free survival (DFS) was reported.
- There is no data as of yet comparing concurrent to sequential anthracycline-taxane therapy (i.e., TAC versus [vs.] doxorubicin and cyclophosphamide (AC) followed by taxane).

**Question #4: Compared with an Anthracycline-Based Regimen, Does a Non-Anthracycline Taxane Regimen Improve Clinically Meaningful Outcomes?**

- For women with early-stage breast cancer, four cycles of three-weekly docetaxel and cyclophosphamide (75/600mg/m<sup>2</sup>) (TC) may not be different than four cycles of three-weekly AC (60/600mg/m<sup>2</sup>); however, data are only available from one randomized trial with short follow-up (see US Oncology [USON] evidence below).

**Question #5: What are the Harms Associated with Adjuvant Taxane Regimens?**

- Given the high rates of febrile neutropenia, prophylactic granulocyte colony-stimulating factor (G-CSF) use in women receiving TAC might be beneficial. The Intergroup Cancer and Leukemia Group B (INT/CALGB) 9741 trial used G-CSF on days three to ten of each cycle at five microgram/kg, which could be rounded to either 300 or 480 microgram total dose, on both arms. This dose is considered a reasonable dose by the Breast Cancer Disease Site Group (DSG).

**General Disclaimer**

- Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult the practice guideline is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or warranties of any kind whatsoever regarding their content or use or application and disclaims any responsibility for their application or use in any way.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better  
Living with Illness

### IOM DOMAIN

Effectiveness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Trudeau M, Eisen A, Messersmith H, Sinclair S, Pritchard K, Breast Cancer Disease Site Group. Adjuvant taxane therapy for women with early-stage, invasive breast cancer. Toronto (ON): Cancer Care Ontario (CCO); 2006 Jan 16. 29 p. (Practice guideline report; no. 1-7). [24 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2006 Jan 16

### GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

### GUIDELINE DEVELOPER COMMENT

The Program in Evidence-based Care (PEBC) is a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

### SOURCE(S) OF FUNDING

Cancer Care Ontario  
Ontario Ministry of Health and Long-Term Care  
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## **GUIDELINE COMMITTEE**

Provincial Breast Cancer Disease Site Group

## **COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE**

For a current list of past and present members, please see the [Cancer Care Ontario Web site](#).

## **FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

The members of the Breast Cancer Disease Site Group (DSG) disclosed potential conflicts of interest relating to the topic of this practice guideline. One of the guideline lead authors (MT) reported related research involvement and funding from Aventis Pharmaceuticals. One author (MT) reported related research involvement and funding from Bristol-Myers Squibb as well as the receipt of honoraria from both companies. In addition, several Disease Site Group members reported related research involvement with those companies.

## **GUIDELINE STATUS**

This is the current release of the guideline.

The EVIDENCE-BASED SERIES, initially the full original Guideline, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the [Cancer Care Ontario Web site](#) for details on any new evidence that has emerged and implications to the guidelines.

## **GUIDELINE AVAILABILITY**

Electronic copies: Available in Portable Document Format (PDF) from the [Cancer Care Ontario Web site](#).

## **AVAILABILITY OF COMPANION DOCUMENTS**

The following are available:

- Adjuvant taxane therapy for women with early-stage, invasive breast cancer. Summary. Toronto (ON): Cancer Care Ontario (CCO), 2006 Jan. Various p. (Practice guideline; no. 1-7). Electronic copies: Available in Portable Document Format (PDF) from the [Cancer Care Ontario Web site](#).
- 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.

## **PATIENT RESOURCES**

None available

## **NGC STATUS**

This summary was completed by ECRI on May 3, 2006. The information was verified by the guideline developer on June 1, 2006.

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