NATIONAL BREAST AND OVARIAN CANCER CENTRE

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RECOMMENDATIONS FOR USE OF

Taxane-containing chemotherapy regimens

for the treatment of early (operable) breast cancer

A CLINICAL PRACTICE GUIDELINE DEVELOPED BY NATIONAL BREAST AND OVARIAN CANCER CENTRE (NBOCC)

This document supplements systemic adjuvant therapy guideline recommendations 12–22 (pp 8–10), specifically those about chemotherapy regimens contained in the National Breast Cancer Centre* *Clinical practice guidelines for the management of early breast cancer*, 2nd edition 2001.[1]

PURPOSE

This guideline includes statements and recommendations based on available, high-level evidence about the use of taxanes in adjuvant and neoadjuvant chemotherapy regimens for the treatment of women with early (operable) breast cancer. The guideline aims to provide health professionals with information to assist in making management recommendations for improved patient outcomes. National Breast and Ovarian Cancer Centre (NBOCC) also develops information specifically for consumers about early breast cancer diagnosis and treatment options.

For information on the Pharmaceutical Benefits Scheme (PBS) listing for taxanes, please see page 18 of this guideline.

Endorsed by:

Faculty of Radiation Oncology

The Royal Australasian College of Physicians

The Royal Australasian College of Surgeons

BACKGROUND

Early (operable) breast cancer is defined as tumours not more than five centimetres in diameter, with either impalpable or palpable but not fixed lymph nodes and with no evidence of distant metastases.[1]

Taxanes are a class of chemotherapy compounds that includes paclitaxel, docetaxel and abraxane. As antimicrotuble agents, taxanes inhibit the normal process of reorganisation of the microtubule network essential for cellular function, which leads to a disruption of mitosis (cell division). Taxanes can be used as part of adjuvant or neoadjuvant chemotherapy regimens to treat early (operable) breast cancer. Of the three types of taxanes, only paclitaxel and docetaxel have been investigated in the adjuvant setting.

SUMMARY OF EVIDENCE

This guideline is based on one meta-analysis[2] about the use of taxane-containing regimens for adjuvant treatment of early breast cancer and a NBOCC systematic review[3] about taxane-containing regimens for neoadjuvant treatment of early breast cancer.

Taxanes for adjuvant treatment of early (operable) breast cancer

The statements and recommendations about taxanes for adjuvant treatment of early breast cancer are based on a Cochrane review and meta-analysis,[2] which includes available evidence from 12 randomised trials[4–15] assessing the adjuvant use of taxanes in early (operable) breast cancer. The trials compared taxane-containing adjuvant chemotherapy regimens with adjuvant regimens not containing a taxane in the management of women with early (operable) breast cancer. Both pre-menopausal and post-menopausal women were eligible in all trials. Five of the twelve trials used paclitaxel.[4,8-11] The remaining seven trials used docetaxel.[5-7,12-15]

(see table 1 on page 8 for trial details)

Taxanes for neoadjuvant treatment of early (operable) breast cancer

The statements about taxanes for neoadjuvant treatment of early breast cancer are based on evidence from a NBOCC systematic review[3] of eight randomised trials[16–23] assessing the neoadjuvant use of taxanes for early (operable) breast cancer.

(see table 3 on page 13 for trial details)

* In February 2008, National Breast Cancer Centre incorporating the Ovarian Cancer Program (NBCC) changed its name to National Breast and Ovarian Cancer Centre (NBOCC)

STATEMENTS AND RECOMMENDATIONS

STATEMENTS	LEVEL OF EVIDENCE[24]	REFERENCE
Adjuvant chemotherapy in women with early (operable) breast cancer:		
Overall and disease free survival benefit		
Inclusion of a taxane in adjuvant chemotherapy regimens improves disease-free and overall survival compared to non-taxane containing regimens	I	Cochrane[2]
Type of taxane		
There are similar benefits for disease-free and overall survival for taxane regimens containing either paclitaxel or docetaxel	I	Cochrane[2]
Schedule and duration of administration		
There are similar benefits for disease-free survival and overall survival for women treated with a taxane-containing regimen regardless of whether the anthracycline is administered sequentially or concurrently with the taxane	I	Cochrane[2]
There are similar benefits for disease-free and overall survival for women treated with a taxane-containing regimen when adding or substituting a taxane as part of a chemotherapy regimen	I	Cochrane[2]
There are similar benefits for disease-free and overall survival for women treated with a taxane-containing regimen: • which is of the same duration as the non-taxane containing regimen, or • which is of longer duration than the non-taxane containing regimen	I	Cochrane[2]

STATEMENTS	LEVEL OF EVIDENCE	REFERENCE
Lymph node status		
There are similar benefits for disease-free survival and overall survival between studies that include women with node positive disease only and studies that include women with node positive or node negative disease No studies have reported results on the use of taxane-containing regimens in women with node negative disease only	I	Cochrane[2]
Hormone receptor status		
There was no level I evidence reporting efficacy of taxanes according to hormone receptor status Results from individual randomised controlled phase III studies are conflicting and no recommendation can be made according to hormone receptor status		
Adverse events		
Taxane-containing regimens are associated with an increased incidence of febrile neutropenia compared with non-taxane-containing chemotherapy regimens The increase in febrile neutropenia is most pronounced in concurrent anthracycline and taxane regimens	I	Cochrane[2]
Taxane-containing chemotherapy regimens are associated with decreased incidence of nausea and vomiting compared with a non-taxane containing chemotherapy regimens The decrease in nausea and vomiting is most pronounced where the inclusion of a taxane has resulted in lower doses of anthracycline	I	Cochrane[2]
Taxane-containing regimens may be associated with a reduction in cardiac toxicity compared with non taxane-containing chemotherapy regimens, where the inclusion of a taxane has resulted in lower cumulative anthracycline exposure	I	Cochrane[2]

STATEMENTS	LEVEL OF EVIDENCE	REFERENCE
Neoadjuvant chemotherapy in women with early (operable) breast cancer:		
One study reported that the inclusion of a taxane in a neoadjuvant chemotherapy regimen significantly increased pathological and clinical complete response rates compared to a non-taxane-containing chemotherapy regimen There is currently insufficient evidence to determine the optimal role of taxane-containing regimens in neoadjuvant chemotherapy treatment	II	NSABP B27[16]

Recommendations to individuals should be based on their risks without taxane-containing chemotherapy regimens, the absolute benefits and harms of treatment, and their preference. These factors should be discussed with the woman. Women receiving a taxane-containing regimen should be reviewed regularly and monitored for adverse effects by clinicians familiar with the drug

RECOMMENDATIONS	LEVEL OF EVIDENCE[24]	REFERENCE
Adjuvant chemotherapy for women with early (operable) breast cancer:		
A taxane-containing regimen should be considered for women at intermediate-to-high risk of breast cancer recurrence	I	Cochrane[2]
The risks and benefits of using a taxane-containing regimen should be discussed with the woman, taking into consideration her individual risk profile and co-morbidities	I	NBCC & NCCI[25]
Optimal schedule of administration		
The optimal scheduling and dosing of taxanes in adjuvant chemotherapy regimens for survival benefits is unknown Decisions on scheduling and dosing of taxane-containing regimens should be based on factors other than survival outcomes, and take into consideration the woman's individual risk profile and co-morbidities— consideration of toxicity effects should guide dosing and scheduling decisions		
Hormone receptor status		
Taxane-containing regimens should be considered as an option regardless of tumour hormone-receptor status	I	Cochrane[2]

RECOMMENDATIONS	LEVEL OF EVIDENCE[24]	REFERENCE
Adverse events		
Women should be informed of the increased risk of febrile neutropenia associated with taxane-containing regimens For women at significant risk of febrile neutropenia, primary prophylaxis with growth factor support should be considered		
Women should be informed of the potential adverse effects of a taxane-containing regimen and any uncertainties about long-term effects	I	Cochrane[2]
Women unsuitable for anthracycline		
If a woman is not suitable to receive an anthracycline-containing regimen, a taxane-containing non-anthracycline regimen can be considered	II	Jones[5]

SUMMARY OF TRIAL RESULTS

ADJUVANT CHEMOTHERAPY

Table 1: Details of the adjuvant trials included in the Cochrane meta-analysis[2]

TRIAL	PATIENT NUMBERS	INTERVENTION	COMPARATOR
CALGB 9344[4]	3121	AC x 4 → P x 4	AC x 4
Jones[5]	1016	DC x 4	AC x 4
BCIRG 001[6]	1491	DAC x 6	FAC x 6
E2197[7]	2889	AD x 4	AC x 4
ECTO[8]	904	AP x 4 → CMF x 4	A x 4 → CMF x 4
GEICAM 9906[9]	1248	FEC90 x 4 → P x 8	FEC90 x 6
HECOG[10]	595	E x 4 → P x 3 → CMF x 4	E x 4 → CMF x 4
NSABP B-28[11]	3059	AC x 4 → P x 4	AC x 4
FinHer[12]	1010	D x 3 (+/- T) → FEC60 x 3	Vin x 3 (+/- T) → FEC60 x 3
PACS 01[13]	1999	FEC100 x 3 → D x 3	FEC100 x 6
Taxit 216[14]	972	E x 4→ D x 4 → CMF x 4	E x 4 → CMF x 3
BIG 2-98[15]	2887	A x 3 → D x 3 → CMF x 3 AD x 4 → CMF x 4	A x 4 → CMF x 3 AC x 4 → CMF x 3

Notes: A=doxorubicin; C=cyclophosphamide; D=docetaxel; E=epirubicin; F=flurouracil; M=methotrexate; P=paclitaxel; T=trastuzumab**;** Vin=vinorelbine

Overall survival

Overall survival data were available for 11 trials. Pooled analyses of the trial results indicated that taxane-containing regimens improved overall survival, with a relative risk reduction of 19% compared to non-taxane-containing control groups ($p<0.00001$).[2] The absolute risk reduction for taxane-containing regimens was ~2.6% compared to non-taxane containing regimens.[2]

Disease-free survival

Disease-free survival data were available for 11 trials. Pooled analyses of the trial results indicated that taxane-containing regimens improved disease-free survival with a relative risk reduction of 19%, compared to non-taxane-containing control groups ($p<0.00001$).[2] The absolute risk reduction for taxane-containing regimens was ~4.1% compared to non-taxane-containing regimens.[2]

Sub-group analysis

Post-hoc analysis of the data by various sub-groups of trials did not alter the overall or disease-free survival estimates,[2] see Table 2 (all remained statistically significant).

Table 2. Overall and disease-free survival sub-group analyses

SUB-GROUP ANALYSIS**	OVERALL SURVIVAL OR (95% CI)	DISEASE-FREE SURVIVAL OR (95% CI)
Overall effect of taxanes	**0.81 (0.75-0.88), p<0.00001**	**0.81 (0.77-0.86), p≤0.00001**
Type of taxane		
Docetaxel	0.76 (0.67-0.86), p<0.0001	0.80 (0.74-0.87), p≤0.00001
Paclitaxel	0.85 (0.76-0.94), p=0.001	0.82 (0.76-0.89), p<0.00001
Taxane given sequentially or concurrently with anthracycline		
Concurrent	0.79 (0.66-0.94), p=0.007	0.79 (0.70-0.90), p=0.0003
Sequential	0.82 (0.75-0.90), p<0.0001	0.81 (0.76-0.88), p<0.00001
Addition or substitution of taxane		
Addition	0.84 (0.76-0.93), p=0.0008	0.82 (0.76-0.89), p≤0.00001
Substitution	0.76 (0.67-0.87), p<0.0001	0.78 (0.71-0.86), p<0.00001
Lymph node status		
Node positive only	0.81 (0.74-0.89), p<0.00001	0.81 (0.76-0.87), p<0.00001
Node positive & negative	0.81 (0.69-0.95), p=0.01	0.80 (0.71-0.91), p=0.0004
Duration of chemotherapy		
Longer duration	0.85 (0.77-0.94), p=0.002	0.83 (0.77-0.90), p<0.00001
Same duration	0.76 (0.67-0.86), p<0.0001	0.77 (0.70-0.85), p<0.00001

Notes: CI=confidence interval; OR=odds ratio
**All sub-group analyses were statistically significant

Scheduling of taxane administration

The Cochrane meta-analysis[2] found statistically significant overall survival and disease-free survival benefits in side-by-side post-hoc analyses that were not altered by scheduling or duration of chemotherapy. Taxane treatment was given either concurrently with anthracycline or sequentially in the trials. Meta-analysis[2] results investigated trial data where there was an 'addition' of a taxane to the control chemotherapy regimen and where the taxane was 'substituted' for part of the control chemotherapy regimen. **Optimal** scheduling of adjuvant taxane-containing chemotherapy regimens is unclear from the available trial results.
The recommendation on scheduling reflects that regardless of how a taxane is used in a chemotherapy regimen, there are overall survival and disease-free survival benefits for women. Results of ongoing trials may provide further evidence for optimal scheduling.

Dose density

Questions regarding dose density were outside the scope of the Cochrane meta-analysis.

HER2 status

There were no available trial data about taxanes and HER2 status at the time of the Cochrane review and meta-analysis[2] (May 2007). Early and retrospective analysis of tissue from the CALGB[26] study (published after March 2007) indicates that the addition of paclitaxel to an adjuvant chemotherapy regimen improved outcomes in HER2 positive women. Further trial results are required to determine definitive recommendations regarding taxanes and HER2 positive early breast cancer patients. This guideline relates specifically to taxanes in adjuvant chemotherapy regimens. It is acknowledged that taxanes have a key role in adjuvant trastuzumab (Herceptin®) trials.

Adverse events

The 12 trials included in the Cochrane review used a variety of control chemotherapies and different dosing and scheduling of the taxane drug. Toxicities need to be considered on a trial-by-trial basis to interpret tolerability of each taxane-containing regimen.

Cardiac toxicity

Pooled analysis of six trials reporting data on cardiotoxicity showed no difference in the risk of cardiotoxicity between taxane-containing and non-taxane-containing regimens. However, for trials in which the use of a taxane resulted in a reduction[8,13] or omission of anthracycline[5], the risk of cardiotoxicity was reduced in the taxane-containing arm (OR 0.38, 95% CI 0.15-0.98, p=0.05).[2]

Febrile neutropenia

Pooled analysis from seven trials demonstrated a significant increase in febrile neutropenia associated with the taxane-containing regimens ($p<0.0001$).[2] The risk was particularly high in the trials that administered the taxane concurrently with an anthracycline, rather than in those that administered sequential taxane and anthracycline treatment.[2]

Other adverse events

Grade III/IV nausea and/or vomiting were less common in the taxane-containing regimens (OR 0.55, 95% CI 0.39-0.77, p=0.0006).[2] There was no difference shown between treatment arms for both grade III/IV fatigue or grade III/IV stomatitis. There was no difference between treatment groups in the number of cases of secondary leukaemia or myelodysplasia reported (25 from taxane-containing regimens, 23 from control regimens). Treatment-related deaths were uncommon and there was no difference between taxane-containing and non-taxane-containing groups (seven treatment-related deaths in each treatment group). There were insufficient and inconsistently reported data for meta-analysis of neurotoxicity or nail changes; however, both toxicities were reported with greater frequency in the taxane-containing arm where reported, with the exception of one study[12] that contained vinorelbine in the control arm and reported greater neurotoxicity in this arm.

Quality of life

Formal analyses of quality of life for patients receiving taxanes are limited, with only two trials reporting on quality of life data. One trial[6] reported that both treatment arms experienced a transient reduction in the quality of life score, with a greater reduction in the taxane-containing regimen. However, at first follow-up, both treatment arms had returned to base-line. The other trial[10] did not demonstrate any difference in quality of life scores between the two treatment arms, either at the beginning or at the end of chemotherapy. Further research is required to determine the short- and long-term effects of taxanes on quality of life.

NEOADJUVANT THERAPY

Evidence is available from eight randomised trials[16–23] assessing the neoadjuvant use of taxanes for early breast cancer. Only one of the trials[16] was large enough to detect survival differences (N=1605), the remaining trials were small, enrolling between 35 and 365 participants. The trials show no significant difference between taxane-containing and non-taxane-containing neoadjuvant chemotherapy regimens for overall, disease-free or relapse-free survival.[16–18,22] There was a trend that taxane-containing regimens achieved higher clinical and pathological response rates compared to non-taxane-containing regimens,[17–23] however, only one trial reported a statistically significant increase.[16] Breast conserving therapy is performed at least as often after taxane-containing neoadjuvant chemotherapy compared to non-taxane-containing neoadjuvant chemotherapy.[16,18,21,22] Toxicity outcomes are not consistently reported in all trials and often the number of events are small, therefore it is difficult to determine whether the toxicity profiles differ significantly between taxane- and non-taxane-containing neoadjuvant regimens. The most commonly, and consistently, reported outcome was febrile neutropenia, with four trials reporting higher rates in the taxane-containing arms compared to the control arms.[16-18,22] Further information is needed to determine the optimal role of neoadjuvant taxanes for treatment of early breast cancer.

Table 3. Details of neoadjuvant trials

TRIAL	PATIENT NUMBERS	INTERVENTION	COMPARATOR
NSABP B-27[16]	1605	AC x 4 → D x 4	AC x 4
MDACC[17]	174	P x 4 → FAC x 4	FAC x 4
Dieras[18]	200	AP x 4 → T	AC x 4 → T
Learn[19]	144	AC x 4 → T → D x 4	AC x 4 → T
Malamos[20]	35	PE x 3	FEC x 3
Lee[21]	78	DC x 4	AC x 4
ACCOG[22]	363	AD x 6	AC x 6
Aberdeen[23]	162	CVAPr x 4 → D x 4	CVAPr x 4 → CVAPr x 4

Notes: A=doxorubicin; C=cyclophosphamide; D=docetaxel; E=epirubicin; F=fluoroucil; P=paclitaxel; Pr=prednisolone; T=tamoxifen; V=vincristine

STRENGTHS AND WEAKNESSES OF EVIDENCE

The trials for adjuvant use of taxanes are large, well designed, and well conducted. Some clinical heterogeneity existed between trials, with variation in choice of control chemotherapy, doses and scheduling of chemotherapy. Post-hoc analyses in a side-by-side comparison of pooled data were performed for a number of subgroups. Information about optimal taxane regimens and efficacy in certain subgroups is not yet available.

Only one trial for neoadjuvant use of taxanes was large enough to detect survival benefits. Future trials and reviews are needed to answer important unanswered questions on neoadjuvant use of taxanes in early breast cancer.

Clinical practice recommendations developed by NBOCC will be reviewed and revised as required as additional significant evidence becomes available.

UNANSWERED QUESTIONS

Important unanswered questions about the use of taxanes in early breast cancer are outlined below; some of these should be addressed in ongoing trials and with longer follow-up of reported trials:

- optimal sequence/timing/duration of adjuvant taxanes with chemotherapy
- optimal use/sequence/timing/duration of neoadjuvant taxanes with chemotherapy
- the relative benefits and harms of different taxanes
- potential long term/late toxicity associated with taxanes
- use of taxanes in patients with node-negative tumours
- use of taxanes in patients with >4 involved axillary lymph nodes
- efficacy of taxanes with regards to hormone receptor status
- efficacy of taxanes with regards to HER2 receptor status
- relative benefits and harms of neoadjuvant use of taxanes compared to adjuvant use
- the short- and long-term effects of taxanes on quality of life.

ONGOING & ADDITIONAL TRIALS

A number of additional phase III trials investigating the adjuvant and neoadjuvant use of taxanes for early breast cancer are ongoing and/or awaiting results:

- eight ongoing trials investigating the use of taxanes for adjuvant treatment of early breast cancer (Brain,[27] GEICAM 9805,[28] Goim 9902,[29] GONO-MIG 5,[30] NCI-H99-0038,[31] NCIC CTG MA.21,[32] PACS 04,[33] ICR TACT[34])
- two ongoing trials investigating the use of taxanes for neoadjuvant treatment of large operable breast cancer (EORTC-10994,[35] INTENS: IKO 2005-01[36])
- one ongoing trial comparing adjuvant treatment to neoadjuvant treatment of taxanes for early breast cancer (ECTO[8]).

REFERENCES

1 National Breast Cancer Centre. Clinical practice guidelines for the management of early breast cancer (2nd Edition). Canberra: Commonwealth of Australia 2001.

2 Ferguson T, Wilcken N, Vagg R, Ghersi D, Nowak AK. Taxanes for adjuvant treatment of early breast cancer. Cochrane Database of Systematic Reviews 2007, Issue 4.

3 National Breast and Ovarian Cancer Centre. Taxanes for neoadjuvant treatment of early breast cancer: a systematic review. National Breast and Ovarian Cancer Centre, Surry Hills, NSW, 2008.

4 Henderson IC, Berry DA, Demetri GD, et al. Improved outcomes from adding sequential paclitaxel but not from escalating doxorubicin dose in an adjuvant chemotherapy regimen for patients with node-positive primary breast cancer. J Clin Oncol 2003;21(6):976–83.

5 Jones SE, Savin MA, Holmes FA, et al. Phase III trial comparing doxorubicin plus cyclophosphamide with docetaxel plus cyclophosphamide as adjuvant therapy for operable breast cancer. J Clin Oncol 2006;24:5381–87.

6 Martin M, Pienkowski T, Mackey J, et al. Adjuvant docetaxel for node-positive breast cancer. N Engl J Med 2005;352:2302–13.

7 Goldstein L. O'Neill A, Sparano J, et al. E2197: phase III AT vs AC in the adjuvant treatment of node positive and high risk node negative breast cancer. J Clin Oncol ASCO Annual Meeting Proceedings 2005;Abstract 512.

8 Gianni L, Baselga J, Eiermann W, et al. European Cooperative Trial in Operable Breast Cancer (ECTO): Improved freedom from progression from adding paclitaxel to doxorubicin followed by cyclophosphamide methotrexate and fluoroucil. J Clin Oncol ASCO Annual Meeting Proceedings 2005;Abstract 513.

9 Martin M, Rodriguez-Lescure A, Ruiz A, et al. Multicentre, randomized phase III study of adjuvant chemotherapy for node positive breast cancer comparing 6 cycles of FEC (90) versus 4 cycles of FEC(90) followed by 8 weekly paclitaxel administrations: interim efficacy analysis of GEICAM 9906 Trial. San Antonio Breast Cancer Symposium 2005;Abstract 39.

10 Fountzilas G, Skarlos D, Dafni U, et al. Postoperative dose-dense sequential chemotherapy with epirubicin, followed by CMF with or without paclitaxel, in patients with high risk operable breast III Oncol 2005;16:1762–71.

11 Mamounas EP, Bryant J, Lembersky B, et al. Paclitaxel after doxorubicin plus cyclophosphamide as adjuvant chemotherapy for node-positive breast cancer: results from NSABP B-28. J Clin Oncol 2005;23:3686–96.

12 Joensuu H, Kellokumpu-Lehtinen P, Bono P, et al. Adjuvant docetaxel or vinorelbine with or without trastuzumab for breast cancer. N Engl J Med 2006;354:809–20.

13 Roche H, Fumoleau P, Spielmann M, et al. Sequential adjuvant epirubicin-based and docetaxel chemotherapy for node-positive breast cancer patients: the FNCLCC PACS 01 Trial. J Clin Oncol 2006;24:5664–71.

14 Bianco AR, De Matteis A, Manzione L, et al. Sequential epirubicin-docetaxel-CMF as adjuvant therapy of early breast cancer: results of the taxit 216 multicenter phase III trial. J Clin Oncol ASCO Annual Meeting Proceedings 2006;24:LBA520.

15 Crown JP, Francis P, Di Leo A. Docetaxel given concurrently with or sequentially to anthracycline-based adjuvant therapy for patients with node-positive breast cancer, in comparison with non-taxane combination chemotherapy. First results of the BIG 2-98 trial at 5 years median follow-up. J Clin Oncol ASCO Annual Meeting Proceedings Part 1 2006;24(18S):LBA519.

16 Bear HD, Anderson S, Smith RE, et al. Sequential preoperative or postoperative docetaxel added to preoperative doxorubicin plus cyclophosphamide for operable breast cancer: National Surgical Adjuvant Breast and Bowel Project Protocol B-27. J Clin Oncol. 2006;24(13):2019–27.

17 Buzdar AU, Singletary SE, Theriault RL, et al. Prospective evaluation of paclitaxel versus combination chemotherapy with fluorouracil, doxorubicin, and cyclophosphamide as neoadjuvant therapy in patients with operable breast cancer. J Clin Oncol. 1999;17(11):3412–7.

18 Dieras V, Fumoleau P, Romieu G, et al. Randomized parallel study of doxorubicin plus paclitaxel and doxorubicin plus cyclophosphamide as neoadjuvant treatment of patients with breast cancer. J Clin Oncol. 2004;22(24):4958–65.

19 Learn PA, Yeh IT, McNutt M, et al. HER-2/neu expression as a predictor of response to neoadjuvant docetaxel in patients with operable breast carcinoma. Cancer. 2005;103(11):2252–60.

20 Malamos N, Kosmas C, Antonopoulos MJ, et al. Prospective randomized study of neoadjuvant chemotherapy (NACT) with paclitaxel/epirubicin (PE) versus fluorouracil/epirubicin/cyclophosphamide (FEC) in operable stage II–IIIA breast cancer (BC). Ann Oncol. 1998;9(4).

21 Lee HG, Lee JJ, Jung KH, et al. Phase III randomized trial of primary chemotherapy with doxorubicin/cyclophosphamide (AC) vs docetaxel/capecitabine (TX) for stage II/III breast cancer (BC): Interim analysis. J Clin Oncol ASCO Meeting 2004;22(14S suppl 15):607.

22 Evans TR, Yellowlees A, Foster E, et al. Phase III randomized trial of doxorubicin and docetaxel versus doxorubicin and cyclophosphamide as primary medical therapy in women with breast cancer: an Anglo-Celtic Cooperative Oncology Group study. J Clin Oncol. 2005;23(13):2988–95.

23 Hutcheon AW, Heys SD and Sarkar TK. Docetaxel primary chemotherapy in breast cancer: a five year update of the Aberdeen trial. Breast Cancer Res Treat. 2003;82(suppl 1):s6.

24 National Health and Medical Research Council. How to use the evidence: assessment and application of scientific evidence. Canberra, Commonwealth of Australia, 2000.

25 National Breast Cancer Centre and National Cancer Control Initiative. Clinical practice guidelines for the psychosocial care of adults with cancer. Canberra: Commonwealth of Australia, 2003.

26 Hayes DF, Thor AD, Dressler LG, et al. HER2 and response to paclitaxel in node-positive breast cancer. N Engl J Med 2007; 357:1496–506.***

27 Brain EGC, Bachelot T, Serin D et al. Phase III trial comparing doxorubicin docetaxel (AT) with doxorubicin cyclophosphamide (AC) in the adjuvant treatment of high-risk node negative (pN0) and limited node positive (pN+</=3) breast cancer (BC) patients (pts): First analysis of toxicity. J Clin Oncol ASCO Annual Meeting Proceedings 2004 22;14S;Abstract 617.

28 Martin M, Lluch A, Segui MA, et al. Prophylactic growth factor support with adjuvant docetaxel, doxorubicin, and cyclophosphamide (TAC) for node-negative breast cancer : An interim safety analysis of the GEICAM 9805 study. J Cl Oncol ASCO Annual Meeting Proceedings 2004 22;Abstract 620.

29 Participating Institutions of Goim 9902 Trial, Italian Cooperative Group, Rome, Italy. Epirubicin and Cyclophosphamide (EC) vs Docetaxel Followed by EC in Adjuvant Treatment of Node Positive Breast Cancer. A Multicenter Randomized Phase III Study. J Clin Oncol, 2001 ASCO Annual Meeting Proceedings. 20; Abstract 1836.

30 Participating Institutions to GONO-MIG 5 study. Absence of Clinically Relevant Cardiotoxicity in Early Breast Cancer Patients Treated with the Association of Epirubicin Plus Paclitaxel: Results from the Italian Mig 5 Study. J Clin Oncol ASCO Annual Meeting Proceedings 2000 19: Abstract 363.

31 National Cancer Institute Clinical Trials (PDQ®) NCI-H99-0038 http://www.cancer.gov/search/ViewClinicalTrials.aspx?cdrid=67305&version=HealthProfessional&protocolsearchid=3554372 Accessed: 22 August 2007.

32 Burnell M, Levine M, Chapman JA, et al. A randomized trial of CEF versus dose dense EC followed by paclitaxel versus AC followed by paclitaxel in women with node positive or high risk node negative breast cancer, NCIC CTG MA.21: Results of an interim analysis. San Antonio Breast Cancer Symposium 2006; Abstract 53.

33 National Cancer Institute Clinical Trials (PDQ®) FRE-FNCLCC-PACS-04/0005 http://www.cancer.gov/search/ViewClinicalTrials.aspx?cdrid=269909&version=HealthProfessional&protocolsearchid=3554380 Accessed: 22 August 2007.

34 National Cancer Institute Clinical Trials (PDQ®) ICR-TACT http://www.cancer.gov/search/ViewClinicalTrials.aspx?cdrid=69311&version=HealthProfessional&protocolsearchid=3554384 Accessed: 22 August 2007.

35 National Cancer Institute Clinical Trials (PDQ®) EORTC-10994 http://www.cancer.gov/clinicaltrials/EORTC-10994 Accessed: 22 August 2007.

36 National Cancer Institute Clinical Trials (PDQ®) INTENS: IKO 2005-01 http://www.cancer.gov/search/ViewClinicalTrials.aspx?cdrid=483044&version=HealthProfessional&protocolsearchid=3554369 Accessed: 22 August 2007.

****This article was considered by the NBOCC's Taxanes Subgroup but published after March 2007*

Membership of NBOCC Taxanes Subgroup

This guideline was developed by a multidisciplinary working group convened by NBOCC

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External Review

NBOCC acknowledges those who gave their time to provide comment on the draft guideline recommendations as part of the external review process

Pharmaceutical Benefits Scheme listing for taxanes; paclitaxel and docetaxel (as of September 2007). For updates after this date, go to http://www.pbs.gov.au

Paclitaxel and docetaxel are currently subsidised for the following indications in the treatment of early breast cancer:

- Paclitaxel—adjuvant treatment of node-positive breast cancer administered sequentially to an anthracycline and cyclophosphamide
- Docetaxel—adjuvant treatment of node-positive breast cancer in combination with an anthracycline and cyclophosphamide
- Paclitaxel and docetaxel—treatment of HER2 positive early breast cancer in combination with trastuzumab

Full details of adjuvant trial results are provided in the Cochrane review *Taxanes for adjuvant treatment of early breast cancer*[2], which can be accessed via the Cochrane Library website: www.cochrane.org

Full details of neoadjunvant trial results are provided in the document *Taxanes for neoadjuvant treatment of early breast cancer: a systematic review*[3], which can be accessed via the NBOCC website: www.nbocc.org.au

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