

OPTIMAL USE OF TAXANES IN METASTATIC BREAST CANCER: SUMMARY

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The recommendations contained in this guideline are a consensus of the Alberta Provincial Breast Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

GUIDELINE GOALS AND OBJECTIVES

To outline the optimal clinical use of taxanes in the management of metastatic breast cancer

GUIDELINE QUESTIONS

- What taxane regimens can be offered to anthracycline-naïve patients with metastatic breast cancer (where HER2 is not over-expressed)?
- What taxane regimens can be offered to anthracycline-pre-treated/resistant patients with metastatic breast cancer (where HER2 is not over-expressed)?
- What taxane regimens can be offered to patients with metastatic breast cancer where HER2 is over-expressed?
- What are the benefits (time to progression, progression free survival, overall survival, quality of life)?
- What are the potential toxicities?

TARGET POPULATION

This guideline is intended for use by chemotherapy-prescribing physicians, nurse practitioners, and pharmacists within Alberta Health Services – Cancer Care and the Alberta Health Services Pharmacy & Therapeutics Committee. The recommendations in this guideline are intended for individuals with metastatic breast cancer (anthracycline naïve or pre-treated/resistant) who are eligible for palliative chemotherapy (hormone refractory and/or rapidly progressive disease, adequate performance status and organ function).

RECOMMENDATIONS

Anthracycline Naïve Patients

1. If single agent chemotherapy is preferred, sequential anthracycline followed by taxane at the time of disease progression, or vice versa, are acceptable alternatives. A survival benefit has not been shown for starting with a taxane.
 - a. The following q3 weekly regimen is recommended: Docetaxel 100 mg/m² every 3 weeks.
 - b. Weekly taxane regimens are also reasonable options if minimization of risk for certain toxicities associated with docetaxel every 3 weeks is desired:
 - i. Docetaxel 35 - 40 mg/m² weekly x3 q4 weeks or weekly x6 q8 weeks.
 - ii. Paclitaxel 80 - 90 mg/m² weekly.
2. If combination chemotherapy is preferred, non-taxane/anthracycline and taxane/anthracycline regimens are acceptable alternatives. Taxane/anthracycline combinations are superior with respect to overall response and progression free survival, but have not been shown to improve overall survival. Additionally, an overall survival benefit for using a taxane/anthracycline combination over planned sequential single agent anthracycline followed by single agent taxane (before disease progression), or at the time of disease progression, has not been shown.

Regarding possible taxane/anthracycline regimens, doublet docetaxel or paclitaxel plus doxorubicin or epirubicin, and triplet docetaxel + doxorubicin + cyclophosphamide have been studied.

Anthracycline Pretreated/Resistant Patients

3. If single agent chemotherapy is preferred, a taxane regimen is recommended. Single agent taxanes appear to improve overall survival and response compared with non-taxane/non-anthracycline regimens.
 - a. The following q3 weekly regimen is recommended: Docetaxel 100 mg/m² every 3 weeks.
 - b. Weekly taxane regimens are also reasonable options if minimization of risk for certain toxicities associated with docetaxel every 3 weeks is desired:
 - i. Docetaxel 35 - 40 mg/m² weekly x3 q4 weeks or weekly x6 q8 weeks.
 - ii. Paclitaxel 80 - 90 mg/m² weekly.
4. If combination chemotherapy is preferred, taxane/non-anthracycline regimens are recommended. Taxane/non-anthracycline regimens are superior with respect to overall survival and response compared with single agent taxanes. Definitive survival data with taxane/non-anthracycline combinations compared with sequential single agent taxane followed by single agent non-taxane/non-anthracycline (at progression) is not available.

The following taxane/non-anthracycline regimens should be options:

- Docetaxel 75 mg/m² day 1 + capecitabine 1250 mg/m² BID days 1-14, q3 weeks.
- Docetaxel 75 mg/m² day 1 + gemcitabine 1000 mg/m² days 1 & 8, q3 weeks.
- Paclitaxel 175 mg/m² day 1 + gemcitabine 1250 mg/m² days 1 & 8, q3 weeks.

Anthracycline naïve or pretreated/resistant patients with paclitaxel or docetaxel intolerance

5. In the setting of an intolerance to paclitaxel or docetaxel (severe infusion reaction considered to be due to the vehicle of the taxanes or severe toxicity from previous administration of a taxane, including corticosteroid intolerance) the following single agent nab-paclitaxel regimens should be options where docetaxel or paclitaxel would otherwise be prescribed:
 - a. Nab-paclitaxel 260-300 mg/m² q3 weeks.
 - b. Nab-paclitaxel 100 - 150 mg/m² weekly x3 q4 weeks.

Anthracycline naïve or pretreated/resistant patients where HER2 is over-expressed

6. A taxane/trastuzumab combination is recommended up front. The addition of trastuzumab to a taxane has been shown to improve overall survival and response. Although the addition of trastuzumab to anthracycline regimens has also been shown to improve overall survival and response, the incidence of cardiac failure is unacceptable. The addition of carboplatin to taxane/trastuzumab combinations has not yet been shown to improve overall survival or consistently increase response.

The strongest evidence is for the following single agent taxane regimens plus weekly trastuzumab:

- Docetaxel 100 mg/m² q3 weeks.
- Paclitaxel 175 mg/m² q3 weeks.

IMPLEMENTATION STRATEGY

- Present the guideline in the tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services website.

EVALUATION STRATEGY

A formal review will be conducted in 2010, however if new evidence is brought forward before that time, the guideline will be changed accordingly.

DECLARATION OF CONFLICT OF INTEREST

None of the authors of this guideline had any conflict of interest related to evidence or recommendations in this guideline.