BC Cancer Protocol Summary for Palliative Therapy for Metastatic Breast Cancer using Weekly PACLitaxel (3 Weeks Out of 4 Weeks Schedule)

***Protocol Code**:* *BRAVTW*
***Tumour Group**:* *Breast*
***Contact Physician**:* *Dr. Stephen Chia*

ELIGIBILITY:

- First, second, or third line treatment of metastatic breast cancer patients with ECOG performance status 0, 1, or 2, and greater than 3 month life expectancy
- Patients unable to tolerate BRAVTAX, such as those with limited marrow reserve, or who are frail and / or elderly

TESTS:

- Baseline: CBC & diff, platelets, bilirubin, ALT
- Baseline if clinically indicated: alk phos, LDH, GGT, CA15-3
- Prior to each treatment: CBC & diff, platelets
- If clinically indicated: bilirubin, ALT

PREMEDICATIONS:

- **PACLitaxel must not be started unless the following drugs have been given**: 45 minutes prior to PACLitaxel:
  - dexamethasone 10 mg IV in 50 mL NS over 15 minutes
  - diphenhydrAMINE 25 mg IV and ranitidine 50 mg IV in 50 mL NS over 20 minutes (compatible up to 3 hours when mixed in bag)

- If no PACLitaxel hypersensitivity reactions occur, no premedications may be needed for subsequent PACLitaxel doses and may be omitted at physician's discretion.
- If hypersensitivity reactions occur, premedications for re-challenge include dexamethasone 20 mg PO given 12 hours and 6 hours prior to treatment, plus IV premedications given 30 minutes prior to PACLitaxel: dexamethasone 10 mg, diphehydrAMINE 25 mg, and H_2-antagonist (e.g., ranitidine 50 mg). If no hypersensitivity reactions occur, standard premedications (see above) will be used for subsequent PACLitaxel doses.

- Additional antiemetics not usually required.

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
PACLitaxel	90 mg/m^2 once weekly x 3 weeks, then 1 week rest	IV in 250 mL NS over 1 hour (use non-DEHP bag and non-DEHP tubing with 0.22 micron or smaller in-line filter)

- Cycle length = 4 weeks, repeat every 28 days for 2-6 cycles
- **Discontinue** if progression or lack of clinical benefit after 3 cycles.

DOSE MODIFICATIONS:

1. Hematological

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose	Dose after Neutropenic Sepsis on PACLitaxel
greater than or equal to 1.5	and	greater than or equal to 100	90 mg/m^2	65 mg/m^2
1.0 to less than 1.5	or	75 to less than 100	65 mg/m^2	50 mg/m^2
less than 1.0	or	less than 75	delay	delay

Note: patients who can not tolerate treatment after 2 dose reductions or require a treatment delay of greater than 2 weeks, should discontinue treatment

2. Non-Hematological Toxicity

Grade	Dose
Grade 2 motor or sensory neuropathy	Decrease dose by 10 mg/m^2
All other grade 2 non-hematological toxicity	Hold treatment until toxicity resolved to less than or equal to grade 1 Decrease subsequent doses by 10 mg/m^2
greater than or equal to Grade 3	Discontinue treatment

Note: patients who cannot tolerate treatment after 2 dose reductions or require a treatment delay of greater than 2 weeks, should discontinue treatment

3. Hepatic Dysfunction

Bilirubin (micromol/L)		ALT	Dose (mg/m^2)
less than or equal to 25	and	less than 2 x ULN	90 mg/m^2
less than or equal to 25	and	greater than or equal to 2 x ULN with no liver metastases or greater than or equal to 5 x ULN with liver metastases	65 mg/m^2
25-50			40 mg/m^2
greater than 50			25 mg/m^2

ULN = upper limit of normal

4. Arthralgia and/or myalgia: If arthralgia and/or myalgia of grade 2 (moderate) or higher is not relieved by adequate doses of NSAIDs or acetaminophen with codeine (e.g., TYLENOL #3®), a limited number of studies report a possible therapeutic benefit using:

- predniSONE 10 mg po bid x 5 days starting 24 hours post-paclitaxel
- gabapentin 300 mg po on day before chemotherapy, 300 mg bid on treatment day, then 300 mg tid x 7-10 days

If arthralgia and/or myalgia persist, reduce subsequent PACLitaxel doses to 65 mg/m^2.

4. Neuropathy: Dose modification or discontinuation may be required (see BC Cancer Drug Manual).

PRECAUTIONS:

1. Hypersensitivity: Reactions to paclitaxel are common. See BC Cancer Hypersensitivity Guidelines.

Mild symptoms (e.g. mild flushing, rash, pruritus)	▪ complete PACLitaxel infusion. Supervise at bedside ▪ no treatment required
moderate symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension	▪ stop PACLitaxel infusion ▪ give IV diphenhydrAMINE 25-50 mg and Hydrocortisone IV 100 mg ▪ after recovery of symptoms resume PACLitaxel infusion at 20 mL/h for 5 minutes, 30 mL/h for 5 minutes, 40 mL/h for 5 minutes, then 60 mL/h for 5 minutes. If no reaction, increase to full rate. ▪ if reaction recurs, discontinue PACLitaxel therapy
severe symptoms (i.e. *one* or more of respiratory distress requiring treatment, generalised urticaria, angioedema, hypotension requiring therapy)	▪ stop PACLitaxel infusion ▪ give IV antihistamine and steroid as above. Add epinephrine or bronchodilators if indicated ▪ discontinue PACLitaxel therapy

2. **Extravasation**: PACLitaxel causes pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
3. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.

Call Dr. Stephen Chia or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Miller K, et al. Paclitaxel plus Bevacizumab versus Paclitaxel alone for metastatic breast cancer. N Engl J Med 2007;357:2666-76.
2. Rugo HS, et al. Randomized phase III trial of weekly paclitaxel compared to weekly nanoparticle albumin bound nab-paclitaxel or ixabepilone with or without bevacizumab as first line therapy for locally recurrent or metastatic breast cancer. J Clin Oncol 2012;30(18)suppl:CRA1002
3. Perez EA, et al. Multicenter phase II trial of weekly paclitaxel in women with metastatic breast cancer. J Clin Oncol 2001;19(22):4216-23.
4. Quock J, et al. Premedication strategy for weekly paclitaxel. Cancer Invest 2002;20(5-6):666-72.
5. Loesch D, et al. Phase II multicenter trial of a weekly paclitaxel and carboplatin regimen in patients with advanced breast cancer. J Clin Oncol 2002;20(18):3857-64. .
6. Wildiers H, Paridaens R. Taxanes in elderly breast cancer patients. Cancer Treat Rev 2004;30(4):333-42.