BCCA Protocol Summary for Palliative Therapy for Metastatic Breast Cancer using Gemcitabine and PACLitaxel

Protocol Code: *BRAVGEMT*

Tumour Group: *Breast*

Contact Physician: *Dr. Vanessa Bernstein*

ELIGIBILITY:

- Progressive symptomatic breast cancer after adjuvant anthracycline-based chemotherapy.
- Second or third line treatment of metastatic breast cancer after previous combination chemotherapy with an anthracycline in patient who has an ECOG status of less than or equal to 2 and a life expectancy greater than three months.
- First line therapy for symptomatic metastatic breast cancer in patient for whom anthracyclines are contraindicated and who has an ECOG status of less than or equal to 2 and a life expectancy greater than three months.
- To continue beyond 6 cycles, an "Individual use of Benefit Drug List Medication for an Undesignated Indication" form must be approved.

TESTS:

- Baseline: CBC & diff, platelets, bilirubin, AST, Creatinine
- Before each treatment: CBC & diff, platelets
- If clinically indicated: Creatinine, bilirubin & AST

PREMEDICATIONS:

- **PACLitaxel must not be started unless the following drugs have been given:**

45 minutes prior to PACLitaxel:

- dexamethasone 20 mg IV in 50 mL NS over 15 minutes

30 minutes prior to PACLitaxel:

- diphenhydrAMINE 50 mg IV and ranitidine 50 mg IV in 50 mL NS over 20 minutes (compatible up to 3 hours when mixed in bag)

- Additional antiemetics not usually required.

TREATMENT:

Drug	Dose	BCCA Administration Guideline
PACLitaxel	175 mg/m^2 on day 1 only	IV in 500 mL* NS over 3 hours (use non-DEHP bag and non-DEHP tubing with 0.22 micron or smaller in-line filter)
gemcitabine	1250 mg/m^2 on day 1 and 8	IV in 250 mL NS over 30 minutes

*use 250 mL for doses less than 150 mg

- Repeat every 21 days x 6 cycles.

- **Discontinue** if no response after 2 cycles.

DOSE MODIFICATIONS:

1. Hematological

Day 1 Counts

ANC ($\times 10^9$/L)		**Platelets ($\times 10^9$/L)**	**Percent of previous cycle day 1 PACLitaxel and gemcitabine dose**
greater than or equal to 1.5	and	greater than or equal to 100	100%
less than 1.5	or	less than 100	Delay 1 week
• Grade 4 febrile neutropenia with previous cycle • Gemcitabine dose adjustment on Day 8 • Greater than 2 week delay of the start of next cycle due to toxicity			75%

Day 8 Counts

ANC ($\times 10^9$/L)		**Platelets ($\times 10^9$/L)**	**Percent Day 1 Gemcitabine Dose**
greater than or equal to 1.2	and	greater than 75	100%
1 to 1.19	or	50 to 75	75%
0.7 to 0.99	and	greater than or equal to 50	50%
less than 0.7	or	less than 50	Hold and reassess on Day 1 next cycle

2. Non-hematologic toxicity (except fatigue & neurotoxicity)

CTC Grade	**Percent of previous cycle day 1 PACLitaxel and gemcitabine dose**
0 to 2 (and grade 3 N+V or alopecia)	100%
3 (except N+V and alopecia)	75% or hold (at discretion of treating MD)
4	50% or hold (at discretion of treating MD)

3. Grade 3 Fatigue

	Percent of previous cycle day 1 PACLitaxel dose
First occurrence	75%
If persistent on 75%	50%
If persistent on 50%	Hold therapy until symptoms less than or equal to grade 1 toxicity. Discontinue PACLitaxel therapy if symptoms do not resolve within 6 weeks.

4. (i) Grade 2 Neurotoxicity

	Percent of previous cycle day 1 PACLitaxel dose
First occurrence	75%
If persistent on 75%	50%
If persistent on 50%	Hold therapy until symptoms less than or equal to grade 1 toxicity. Discontinue PACLitaxel therapy if symptoms do not resolve within 6 weeks.

(ii) Grade 3 Neurotoxicity

	Percent of previous cycle day 1 PACLitaxel dose
Any occurrence	Hold therapy until symptoms less than or equal to grade 1 toxicity. Discontinue PACLitaxel therapy if symptoms do not resolve within 6 weeks.
Recovery to grade less than or equal to 1	Reinstitute at 50% (MD can escalate dose at their discretion)
No Recovery to grade less than or equal to 1	Discontinue PACLitaxel

5. Hepatic Dysfunction

Bilirubin (micromol/L)		AST	Dose PACLitaxel
less than or equal to 25	and	less than 2x ULN	175 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	135 mg/m^2
25 to 50	and	less than or equal to 10 x ULN	75 mg/m^2
greater than 50	or	greater than 10 x ULN	Not recommended

ULN = upper limit of normal

6. 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 to 10 days

If arthralgia and/or myalgia persist, reduce subsequent PACLitaxel doses to 135 mg/m^2.

PRECAUTIONS:

1. **Hypersensitivity**: Reactions are common. See BCCA 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 to 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 BCCA Extravasation Guidelines.
3. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
4. **Renal Dysfunction**: Irreversible renal failure associated with hemolytic uremic syndrome may occur (rare). Use caution with pre-existing renal dysfunction.
5. **Pulmonary Toxicity**: Acute shortness of breath may occur. Discontinue treatment if drug-induced pneumonitis is suspected.
6. **Possible interaction with warfarin has** been reported and may occur at any time. Close monitoring is recommended (monitor INR weekly during gemcitabine therapy and for 1 to 2 months after discontinuing gemcitabine treatment).

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

Date activated: 1 October 2005
Date revised: 1 Jul 2017 (Drug interaction with warfarin updated)