

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.
- Class II form must be completed for first 6 cycles. For further 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-PVC equipment, 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 (x 10 ⁹ /L)		Platelets (x 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
<ul style="list-style-type: none">Grade 4 febrile neutropenia with previous cycleGemcitabine dose adjustment on Day 8Greater than 2 week delay of the start of next cycle due to toxicity			75%

Day 8 Counts

ANC (x 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	Percent Day 1 Gemcitabine Dose
greater than or equal to 1.2	and	greater than 75	100%
1.0 - 1.19	or	50-75	75%
0.7-.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
0-2 (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
25-50	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 7-10 days

If arthralgia and/or myalgia persist, reduce subsequent Paclitaxel doses to 135 mg/m².

PRECAUTIONS:

1. **Hypersensitivity:** Reactions are common. See BCCA Hypersensitivity Guidelines.

<i>Mild</i> symptoms (e.g. mild flushing, rash, pruritus)	<ul style="list-style-type: none"> ▪ Complete Paclitaxel infusion. ▪ Supervise at bedside ▪ No treatment required
<i>moderate</i> symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension)	<ul style="list-style-type: none"> ▪ 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
<i>severe</i> symptoms (i.e. <u>one</u> or more of respiratory distress requiring treatment, generalised urticaria, angioedema, hypotension requiring therapy)	<ul style="list-style-type: none"> ▪ 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.

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 May 2009 (unsafe abbreviations and symbols replaced)