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

Protocol Code *BRAVGEMP*

Tumour Group *Breast*

Contact Physician *Dr. Susan Ellard*

ELIGIBILITY:

- Progressive breast cancer after adjuvant anthracycline-based chemotherapy.
- Second or third line treatment of metastatic breast cancer after previous chemotherapy with an anthracycline in a 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 a 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.
- adequate hematologic, hepatic, and renal function
- To continue beyond 8 cycles, a BCCA "Compassionate Access Program" request must be approved.

EXCLUSIONS:

- Patients with poor renal function (creatinine clearance less than 60 ml/min by GFR measurement or Cockcroft formula)
- Major co-morbid illness

TESTS:

- Baseline: CBC & differential, platelets, creatinine, liver function tests, bilirubin
- Before each treatment:
  - Days 1: CBC & differential, platelets, creatinine, liver function tests, bilirubin
  - Day 8: CBC & differential, platelets, creatinine

PREMEDICATIONS:

- Antiemetic protocol for high moderate emetogenic chemotherapy protocols (see protocol SCNAUSEA).

TREATMENT:

Drug	Dose	BCCA Administration Guideline
gemcitabine	750* mg/m^2/day on Day 1 and 8	IV in 250 mL NS over 30 min
CISplatin	30 mg/m^2/day on Day 1 and 8	IV in 500 mL NS 45 minutes

*starting dose of 600 mg/m^2/day recommend for patients who have received 2 or more prior chemotherapy regimens

Repeat every 21 days x 6 cycles. Discontinue if no response after 2 cycles.
If patient still receiving benefit after 6 cycles, further 2 cycles may be given.
To continue beyond 8 cycles, a BCCA "Compassionate Access Program" request must be approved.

DOSE MODIFICATIONS:

1. **Hematology**

For gemcitabine day 1 of each cycle

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose
greater than or equal to 1	and	greater than 100	100%
0.5 to 0.99	or	75 to 100	75%
less than 0.5	or	less than 75	***Delay****
CISplatin also delayed			

For gemcitabine day 8 of each cycle

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose**
greater than or equal to 1	and	greater than 100	100%
0.5 to 0.99	or	75 to 100	75%
less than 0.5	or	less than 75	***Omit***
****Dose adjustment only for the day of treatment the CBC is drawn**			

2. **Renal Dysfunction**

Creatinine Clearance (ml/min)	CISplatin dose	Gemcitabine dose
greater than or equal to 60	30 mg/m^2 on Day 1 and 8	100%
45 to 59	80% CISplatin or go to CARBOplatin option	100%
less than 45	***Delay***	***Delay/omit ****
****Delay if day 1; if day 8, omit if <u>serum</u> creatinine greater than 3 x ULN where ULN = local upper limit of normal range.***		

Alternatively, CARBOplatin may be used instead of CISplatin, with reduced gemcitabine dose:

Drug	Dose	BCCA Administration Guideline
gemcitabine	600 mg/m^2/day on days 1 and 8	IV in 250 mL NS over 30 min
CARBOplatin	AUC 5 DAY 1 only Dose = AUC x (GFR* +25)	IV in 250mL NS over 30 minutes.

* *<u>Measured GFR</u>* (e.g. nuclear renogram) is preferred whenever feasible, *<u>particularly</u>* in circumstances of co-morbidity that could affect renal function (third-space fluid accumulations, hypoproteinemia, potentially inadequate fluid intake, etc.). The lab reported GFR (MDRD formula) may be used as an alternative to the Cockcroft-Gault estimate of GFR.

Cockcroft-Gault Formula

$$\text{GFR} = \frac{\text{N* x (140 - age in years) x wt (kg)}}{\text{serum creatinine (micromol/L)}}$$

Note: The *<u>same</u>* method of estimation should be used throughout the treatment course (i.e. if lab reported GFR was used initially, this should be used for dosing in all subsequent cycles and not the Cockcroft-Gault estimate).

*For males in = 1.23; for females N = 1.04

Other Toxicities: for gemcitabine only

Grade	Stomatitis	Diarrhea	Dose
1	Painless ulcers, erythema or mild soreness	Increase of 2 to 3 stools/day	100%
2	Painful erythema, edema, or ulcers but can eat	Increase of 4 to 6 stools, or nocturnal stools	Omit until toxicity resolved then resume at 100%
3	Painful erythema, edema, or ulcers and cannot eat	Increase of 7 to 9 stools/day or incontinence, malabsorption	Omit until toxicity resolved then resume at 75%
4	Mucosal necrosis, requires parenteral support	Increase of greater than or equal to 10 stools/day or grossly bloody diarrhea requiring parenteral l support	Omit until toxicity resolved then resume at 50%

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Irreversible renal failure associated with hemolytic uremic syndrome may occur (rare) with gemcitabine. Use caution with pre-existing renal dysfunction.
3. **Pulmonary Toxicity**: Acute shortness of breath may occur. Discontinue treatment if drug-induced pneumonitis is suspected.
4. **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).

Contact Dr. Susan Ellard or tumour group delegate at (250) 712-3900 or 1-888-563-7773 with any problems or questions regarding this treatment program.

Date activated: 01 June 2007 (as UBRAVGEMP)

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

References:

Nagourney, R., et al. Gemcitabine plus cisplatin repeating doublet therapy in previously treated, relapsed breast cancer patients. J Clin Oncol 2000;18(11):2245-2249.