BC Cancer Protocol Summary for Palliative Therapy for Metastatic Breast Cancer using eriBULin

Protocol Code	***BRAVERIB***
Tumour Group	***Breast***
Contact Physician	***Dr Stephen Chia***

ELIGIBILITY:

- treatment of metastatic or incurable locally advanced breast cancer patients meeting the following criteria:
  - previous treatment with a taxane and an anthracycline in either the adjuvant or advanced setting
  - at least two chemotherapy regimens for metastatic or locally recurrent disease
  - who have progressed after their last therapy
  - may have received TWO of the following as monotherapy or in combination prior to eriBULin: capecitabine, vinorelbine or gemcitabine (but not all 3 agents). Please note that BC Cancer does NOT approve the use of all four of these agents (eriBULin, vinorelbine, gemcitabine and capecitabine) in this setting, only 3 agents will be approved.
- ECOG status of less than or equal to 2
- life expectancy of 3 months or more
- adequate hematological, renal and hepatic function

EXCLUSIONS:

- pregnancy
- severe pre-existing peripheral neuropathy

TESTS:

- Baseline: CBC & diff, platelets, bilirubin, GGT, alk phos, ALT, LDH, serum creatinine, sodium, potassium
- Prior to Day 1 treatment: CBC & diff, platelets, sodium, potassium, serum creatinine, bilirubin, GGT, alk phos, ALT, LDH,
- Prior to Day 8 treatment: CBC & diff, platelets, serum creatinine
- Baseline and routine ECGs for patients at risk of developing QT prolongation (at the discretion of the ordering physician)
- If clinically indicated: total protein, albumin, BUN

PREMEDICATION:

- Antiemetic protocol for low emetogenic chemotherapy (see protocol SCNAUSEA)

TREATMENT:

Drug	Dose*	BC Cancer Administration Guideline
eriBULin	1.4 mg/m^2/day on days 1 and 8	IV Push over 2 to 5 minutes

Repeat every 21 days. Continue until disease progression, no evidence of further response or unacceptable toxicity.

*Dose Levels

Starting Dose	Dose level -1	Dose level -2	Dose level -3
1.4 mg/m^2	1.1 mg/m^2	0.7 mg/m^2	discontinue

DOSE MODIFICATIONS:

1. **Hematological and other non-hematological toxicities:**
   - patients should have a baseline ANC greater than 1.5 x 10^9/L and platelets greater than 100 x 10^9/L prior to their first dose of eriBULin
   - myelosuppression is dose dependent and primarily manifested as neutropenia
   - febrile neutropenia occurred in approximately 5% of patients receiving eriBULin
   - do not re-escalate dose after dose reduction

On Treatment: Day 1 and 8

ANC x 10^9/L		Platelets x 10^9/L	Dose
greater than or equal to 1.0	and	greater than or equal to 75	100%
less than 1.0	or	less than 75	delay 1 week & repeat CBC*

*Day 8 dose may be delayed for 1 week, if no recovery omit for that cycle, if toxicities resolve or improve to less than or equal grade 2 by Day 15, administer at a reduced dose level and initiate next cycle no sooner than 2 weeks later

2. Additional Hematological and Non-Hematological

Event Description	Dose
Permanently reduce from 1.4mg/m^2 for any of the following toxicities: • ANC less than 0.5 x 10^9 for greater than 7 days • ANC less than 1.0 x 10^9 with fever or infection • Platelets less than 25 x 10^9 • Platelets less than 50 x 10^9 requiring transfusion • non-hematologic grade 3 or 4 toxicities • omission or delay of day 8 dose in previous cycle for toxicity	**1.1 mg/m^2**
If any of the above events occurs while receiving 1.1mg/m^2	**0.7 mg/m^2**
If any of the above events occurs while receiving 0.7 mg/m^2	**discontinue**

3. Renal Dysfunction

Creatinine Clearance (mL/min)	Dose on Day 1 and 8
greater than 50	1.4 mg/m^2
15-50	1.1 mg/m^2
less than 15	no data; not recommended

4. Hepatic Impairment

Hepatic Impairment	Recommended Dose on Day 1 and 8
Normal (bilirubin less than 1.5 x ULN, transaminases less than or equal to 3 x ULN	1.4 mg/m^2
Mild (Child-Pugh A)	1.1 mg/m^2
Moderate (Child-Pugh B)	0.7 mg/m^2
Severe (Child-Pugh C)	not recommended

Note: physician should assess hepatic function prior to starting treatment to ensure adequate for treatment

PRECAUTIONS:

1. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **QT/QTc interval prolongation** has been observed with eriBULin. Baseline and periodic ECG and electrolyte monitoring are suggested in patients at risk for developing torsades de pointes including those with cardiac disease, history of arrhythmias, electrolyte disturbances, nutritional deficits, etc. Concurrent therapy with other QT/QTc-prolonging drugs may increase the risk of potentially fatal arrhythmias; avoid if possible.

Call Dr. Stephen Chia or tumour group delegate at (604) 877-6000 or 1-888-563-7773 with any problems or questions regarding this treatment program.

References:

Cortes J, O'Shaughnessy J, Loesch D, et al. Eribulin monotherapy versus treatment of physician's choice in patient with metastatic breast cancer (EMBRACE): a phase 3 open-label randomized study. Lancet 201 3; 377:914-23.