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

Protocol Code	*SAAVERIB*
Tumour Group	*Sarcoma*
Contact Physician	*Dr. Christine Simmons*

ELIGIBILITY:

- Incurable locally recurrent, locally advanced, or metastatic liposarcoma or leiomyosarcoma, meeting the following criteria:
  - previous treatment with at least two chemotherapy regimens for advanced disease, including an anthracycline (unless contraindicated)
  - disease not amenable to curative surgery or radiotherapy
- ECOG status of less than or equal to 2
- Adequate hematological, renal and hepatic function

EXCLUSIONS:

- pregnancy
- severe pre-existing peripheral neuropathy
- patients with congenital long QT/QTc syndrome. NOTE: The concomitant use of eriBULin with another QT/QTc-prolonging drug should be avoided

TESTS:

- Baseline: CBC & differential, platelets, total bilirubin, albumin, INR (if clinically indicated), ALT, alkaline phosphatase, creatinine, sodium, potassium, calcium, magnesium
- Prior to Day 1 treatment: CBC & differential, platelets, total bilirubin, ALT, alkaline phosphatase, creatinine, sodium, potassium
- Prior to Day 8 treatment: CBC & differential, platelets, 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, INR, BUN, calcium, magnesium

PREMEDICATIONS:

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

TREATMENT:

Drug	Dose*	BC Cancer Administration Guideline
eriBULin	1.4 mg/m2 /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: Days 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 to 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. Christine Simmons or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Schöffski P, Chawla S, Maki RG, et al. Eribulin versus dacarbazine in previously treated patients with advanced liposarcoma or leiomyosarcoma: a randomised, open-label, multicentre, phase 3 trial. *Lancet*. 2016;387(10028):1629–1637. doi:10.1016/S0140-6736(15)01283-0