BC Cancer Protocol Summary for Metastatic or Unresectable Angiosarcoma using Weekly PACLitaxel (3 Weeks out of 4 Weeks Schedule)

Protocol Code:	*SAAVTW*
Tumour Group:	*Sarcoma*
Contact Physician:	*Dr. Xiaolan Feng*

ELIGIBILITY:

- Metastatic or unresectable angiosarcoma
- ECOG performance status 0 or 1
- *Note: Patients are eligible to receive weekly paclitaxel OR doxorubicin infusion but not sequential use of these agents*

TESTS:

- Baseline: CBC & differential, platelets, total bilirubin, ALT, creatinine
- Baseline if clinically indicated: alkaline phosphatase, LDH, GGT
- Prior to each treatment: CBC & differential, platelets
- If clinically indicated: total bilirubin, ALT, alkaline phosphatase, creatinine

PREMEDICATIONS:

- **PACLitaxel must not be started unless the following drugs have been given**:
  45 minutes prior to PACLitaxel:
  - dexamethasone 10 mg IV in 50 mL NS over 15 minutes

  30 minutes prior to PACLitaxel:
  - diphenhydrAMINE 25 mg IV in 50 mL NS over 15 minutes and famotidine 20 mg IV in 100 mL NS over 15 minutes (Y-site compatible)

- If no PACLitaxel infusion reactions occur, no premedications may be needed for subsequent PACLitaxel doses and may be omitted at physician's discretion.
- If infusion reactions occur, premedications for re-challenge include dexamethasone 20 mg PO given 12 hours and 6 hours prior to treatment, plus IV premedications given 30 minutes prior to PACLitaxel: dexamethasone 10 mg, diphenhydrAMINE 25 mg, and H_2-antagonist (e.g., famotidine 20 mg). If no infusion reactions occur, standard premedications (see above) will be used for subsequent PACLitaxel doses.

- Additional antiemetics not usually required.

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
PACLitaxel	80 mg/m^2 once weekly x 3 weeks, then 1 week rest	IV in 100 to 500 mL NS over 1 hour (use non-DEHP bag and non-DEHP tubing with 0.2 micron in-line filter)

- Cycle length = 4 weeks, repeat every 28 days x 6 cycles
- **Discontinue** if progression, or unacceptable toxicity.

DOSE MODIFICATIONS:

1. Hematological Toxicity

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose	Dose after Neutropenic Sepsis on PACLitaxel
greater than or equal to 1.0	and	greater than or equal to 100	80 mg/m^2	70 mg/m^2
less than 1.0	or	less than 100	Contact Physician: Delay treatment. Reduce next dose to 70 mg/m^2 After a second episode, reduce subsequent doses to 60 mg/m^2	delay

Note: patients who cannot tolerate treatment after a dose reduction or require a treatment delay of greater than 3 weeks, should discontinue treatment.

2. Non-Hematological Toxicity

Grade	Dose
Grade 2 motor or sensory neuropathy	Decrease dose by 10 mg/m^2
All other grade 2 non-hematological toxicity	Hold treatment until toxicity resolved to less than or equal to grade 1 Decrease subsequent doses by 10 mg/m^2
greater than or equal to Grade 3	Discontinue treatment

Note: patients who cannot tolerate treatment after 2 dose reductions or require a treatment delay of greater than 2 weeks, should discontinue treatment

3. Hepatic Dysfunction

Bilirubin (micromol/L)		ALT	Dose
less than 3 x ULN	and	less than 2.5 x ULN	80 mg/m^2
Greater than or equal to 3 x ULN	and	greater than or equal to 2.5 x ULN	70 mg/m^2

ULN = upper limit of normal

4. 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 50 to 70 mg/m^2, as per clinician's discretion.

5. Neuropathy: Dose modification or discontinuation may be required (see BC Cancer Drug Manual).

PRECAUTIONS:

1. **Infusion-related reactions**: Reactions to paclitaxel are common. See BC Cancer Infusion-Related Reactions 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 25-50 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 BC Cancer Extravasation Guidelines.
3. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.

Call Dr. Xiaolan Feng or tumour group delegate at 250-519-5500 or 1-800-670-3322 with any problems or questions regarding this treatment program.

References:

1. Italiano A, Cioffi A, Penel N, et al. Comparison of doxorubicin and weekly paclitaxel efficacy in metastatic angiosarcomas. Cancer 2012;118(13):3330-6.
2. Penel N, Bui BN, Bay JO, et al. Phase II trial of weekly paclitaxel for unresectable angiosarcoma: the ANGIOTAX study. J Clin Oncol 2008;26:5269–74
3. Ray-Coquard IL, Domont J, Tresch-Bruneel E, et al. Paclitaxel given once per week with or without bevacizumab in patients with advanced angiosarcoma: a randomized phase II trial. J Clin Oncol 2015;33:2797–802.