BC Cancer Protocol Summary for 3-day DOXOrubicin – ifosfamide - mesna for use in Patients with Advanced Soft Tissue Sarcoma

Protocol Code	*SAAI3*
Tumour Group	*Sarcoma*
Contact Physician	*Dr. Xiaolan Feng*

ELIGIBILITY:

- Patients with locally advanced or metastatic soft tissue sarcoma
- Good performance status
- Adequate bone marrow, renal and hepatic function (bilirubin less than 2 x ULN)

TESTS:

- Baseline and before each treatment: CBC & diff, platelets, electrolytes panel, calcium, albumin, creatinine, bilirubin, ALT, and clinical measure of tumour response.
- Urine dipstick for blood before each treatment as well as q 8 hours – if positive at any time, notify doctor, send urine sample for urinalysis for verification and accurate measurement of hematuria and refer to supportive care protocol SCMESNA (follow SCMESNA (SAAI) preprinted order - ifosfamide dose to be given over 2 days)
- If clinically indicated: chest x-ray or other imaging to monitor response

PREMEDICATIONS:

- **ondansetron** 8 mg PO/IV 30 to 60 minutes pre-chemotherapy on day 1, then 8 mg PO/IV every 8 hours x 8 doses post-chemotherapy
- **dexamethasone** 8 mg PO/IV 30 to 60 minutes pre-chemotherapy on day 1, then 4 mg PO/IV every 12 hours x 5 doses post-chemotherapy
- **aprepitant** 125 mg PO 30 to 60 minutes pre-chemotherapy on day 1, then 80 mg PO daily on day 2 and 3
- **LORazepam** 1 mg SL every 4-6 hours prn for nausea, sleep or restlessness
- **prochlorperazine** 10 mg PO every 4-6 hours prn for nausea or vomiting

TREATMENT: Day 1, 2, 3 of a 21 day cycle

Hour	Drug	Dose	BC Cancer Administration Guide
0 to 1	Pre-hydration: NS	500 mL/h	IV in 500 mL over 1 h
	DOXOrubicin	25 mg/m2	IV push
1 to 1.25	mesna	600 mg/m²	IV in 100 mL NS over 15 min
1.25 to 5.25	ifosfamide*†	3000 mg/m^2	IV in 500 mL NS over 4 h To be y-sited
	mesna†	3000 mg/m^2	IV in 500 mL NS over 4 h
5.25 to 5.75	Post-hydration: NS	250 mL/h	IV in 250mL over 30 minutes
5.75 to 6	mesna**	600 mg/m^2	IV in 100 mL NS over 15 min
		or	
		1200 mg/m²	PO in carbonated beverage as outpatient

* Total cumulative dose of ifosfamide generally should not exceed 72000 mg/m² as there is an increased risk of Renal Fanconi Syndrome in children.
** If tolerated, may use oral mesna for last day of inpatient SAAI3 to allow for more timely discharge
† Ifosfamide and Mesna infused concurrently via Y- site connector placed immediately before injection site

Repeat every 21 days for a total of 6 cycles.

DOSE MODIFICATIONS:

1. **Hematological**:

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose (all drugs)
greater than or equal to 1.5	and	greater than or equal to 100	100 %
1.0 to less than 1.5	or	70 to less than 100	80 %
less than 1.0	or	less than 70	Delay one week

2. **Renal Dysfunction:** If Day 1 serum creatinine increases greater than 100% or is greater than ULN, calculate creatinine clearance to determine whether ifosfamide should be discontinued:

$$\text{Creatinine clearance} = \frac{N^* \times (140 - \text{Age}) \times \text{Weight (kg)}}{\text{Serum creatinine}}$$

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

CrCl (ml/min)	Treatment Guidelines
greater than or equal to 50	Continue with ifosfamide
less than 50	Discontinue treatment with ifosfamide

If renal function does not return to normal between cycles, **give DOXOrubicin as a single agent for any further cycles.**

If Ifosfamide is discontinued mid-cycle because of decreasing renal function, mesna infusion should be continued at a dose of 1250 mg/m^2 for 48 hours following ifosfamide discontinuation.

3. **Mucositis:** Grade 3 or 4, reduce dose of all drugs to 80%
4. **Nausea & Vomiting:** Grade 4 despite optimal use of antiemetics, reduce dose of all drugs to 80% or QUIT
5. **Neutropenic Fever** (with ANC less than 0.5 x 10^9/L): Once counts have recovered, reduce dose of all drugs to 80%
6. **Hepatic Dysfunction:** For bilirubin 1.5 - 2 times ULN, reduce dose of DOXOrubicin to 50%

PRECAUTIONS:

1. **Hematuria:** Refer to supportive care protocol SCMESNA (see SCMESNA (SAAI) preprinted order)
2. **CNS Toxicity:** Ifosfamide can cause encephalopathy with symptoms of drowsiness, hallucinations, confusion, seizures and coma. If drowsiness develops while receiving ifosfamide, discontinue all sedating medications and continue ifosfamide. If patient is confused, unarousable or comatose, discontinue ifosfamide. If ifosfamide is the cause of CNS depression, then it should not be given again. If the CNS changes are not due to ifosfamide, then ifosfamide can be reinstituted providing the previous

medications contributing to CNS toxicity are not given again with it. If a seizure occurs on ifosfamide, then that cycle is to be discontinued. Further cycles may be given if the patient is on anticonvulsants.

3. **Cardiac Toxicity:** DOXOrubicin is cardiotoxic and must be used with caution, if at all, in patients with severe hypertension or cardiac dysfunction. Cardiac assessment is recommended if lifelong dose of 450 mg/m^2 to be exceeded. Refer to BC Cancer Drug Manual.
4. **Extravasation:** DOXOrubicin causes pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
5. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.

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.