BC Cancer Protocol Summary for Ifosfamide for Use in Patients with Advanced Soft Tissue Sarcoma

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

ELIGIBILITY:

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

EXCLUSIONS:

- Untreated obstructive uropathy
- Extreme hypoalbuminemia
- Caution – solitary kidney

TESTS:

- Baseline and before each treatment: CBC & diff, platelets, electrolytes panel, creatinine, calcium, bilirubin, ALT, alk phos, GGT, LDH, albumin 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 determination of hematuria and refer to supportive care protocol SCMESNA (follow SCMESNA (SAAVI) 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
- **dexamethasone** 8 mg PO/IV 30 to 60 minutes pre-chemotherapy, then 4 mg PO/IV every 12 hours x 2 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:

Drug	Dose	BC Cancer Administration Guideline
mesna	600 mg/m^2	IV in 100 mL NS over 15 minutes
ifosfamide	5000 mg/m^2/day	IV in 3 L of NS with mesna 2500 mg/m^2 to infuse over 24 h. Total dose of ifosfamide to be divided equally between three 1 L bags with each litre to be run over 8 h. Total dose of mesna to be divided equally between two 1 L bags with each litre to be y-sited to ifosfamide and run over 12 h.
mesna	1250 mg/m^2	IV in 1 L of NS to infuse over 12 h
furosemide	20 mg	IV at hour 16 and 28

Repeat every 21 days

DOSE MODIFICATIONS:

1. **Hematological:**

ANC (x10^9/L)		Platelets (x10^9/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, estimate creatinine clearance using the formula:

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

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

Cr_{Cl} (mL/min)	
greater than or equal to 50	Continue with ifosfamide
less than 50	Discontinue treatment with ifosfamide

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. **Nausea & Vomiting**: Grade 4 despite optimal use of anti-emetics, reduce dose of all drugs to 80% or QUIT

4. **Febrile Neutropenia** (with ANC less than 0.5 x 10^9/L): Once counts have recovered, reduce dose of all drugs to 80%

PRECAUTIONS:

1. **Hematuria:** Refer to supportive care protocol SCMESNA – (see SCMESNA (SAAVI) preprinted order - **ifosfamide to be given over 2 days**)
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 reinstitued 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. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.

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: