BC Cancer Protocol Summary for 3-day Ifosfamide for Use in Patients with Advanced Soft Tissue Sarcoma

Protocol Code	*SAAVI3*
Tumour Group	*Sarcoma*
Contact Physician	***Dr. Xiaolan Feng***

ELIGIBILITY:

- Patients with an advanced soft tissue sarcoma
- Good performance status
- Adequate bone marrow, renal and hepatic function (bilirubin less than 2 x ULN)
- To be used only when SAAVI delivery not feasible

EXCLUSIONS:

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

TESTS:

- Baseline and before each treatment: CBC & diff, platelets, sodium, potassium, creatinine, calcium, bilirubin, ALT, alk phos, GGT, LDH, albumin and clinical measure of tumour response
- If Day 1 CBC & diff or creatinine levels are ABNORMAL, recheck CBC & diff or creatinine on Day 3. Notify doctor of results prior to administering chemotherapy on Day 3
- 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 (SAAVAI3) preprinted order.
- 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 12 hours for 5 doses
- **dexamethasone** 8 mg PO/IV 30 to 60 minutes pre-chemotherapy on Day 1, then 4 mg PO/IV every 12 hours for 5 doses
- **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 as needed
- **prochlorperazine** 10 mg PO every 4-6 hours as needed

TREATMENT: Days 1, 2 & 3 of a 21-day cycle

Hour	Drug	Dose	BC Cancer Administration Guide
0 to 1	NS	500 mL/h	
1 to 1.25	mesna	600 mg/m²	IV in 100 mL NS over 15 min
1.25 to 5.25	ifosfamide*†	3000 mg/m²	IV in 500 mL NS over 4 h To be y-sited
	mesna†	1500 mg/m²	IV in 500 mL NS over 4 h
5.25 to 9.25	After completion of ifosfamide infusion: • For patients receiving mesna by **IV**, continue hydration with NS IV at 250 mL/h until after Hour 9.25 mesna. • For patients receiving mesna **orally**, no further hydration needed.		
9.25 and 13.25	mesna**	600 mg/m²	IV in 100 mL NS over 15 min
		or	
		1200 mg/m²	PO in carbonated beverage as outpatient
9.25	NS IV at 150 mL/h for 8 hours • For patients who are hydrating well and have not had hematuria, IV hydration may be discontinued daily after Hour 9.25 mesna bolus. • ONLY patients with hematuria requiring mesna dose adjustments are required to be treated on a 24 hour schedule.		

* 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 SAAVI3 to allow for more timely discharge
† Ifosfamide and Mesna infused concurrently via Y- site connector placed immediately before injection site

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 than100	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

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

If ifosfamide is discontinued mid-cycle, continue with mesna for 48 hours.

3. **Nausea & Vomiting**: Grade 4 despite optimal use of anti-emetics, reduce dose of all drugs to 80% or discontinue treatment.
   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 (SAAVI3) 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, not arousable 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. 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:

van Oosterom AT, et al. Results of randomised studies of the EORTC Soft Tissue and Bone Sarcoma Group (STBSG) with two different ifosfamide regimens in first- and second-line chemotherapy in advanced soft tissue sarcoma patients. Eur J Cancer 2002;38(18):2397-406.