

BC Cancer Protocol Summary for Etoposide, Ifosfamide-Mesna (SAIME) for Use in Sarcomas

Protocol Code	<i>SAIME</i>
Tumour Group	<i>Sarcoma</i>
Contact Physician	<i>Dr. Christine Simmons</i>

ELIGIBILITY:

- Advanced soft tissue sarcomas of adult, pediatric and bone type
- Normal kidney, cardiac and hepatic function
- **Newly diagnosed Ewing sarcoma/Ewing family of tumours, intra-abdominal small round blue cell tumour or rhabdomyosarcoma or high grade small round blue cell tumours in the adolescent/young Adult age group (less than 30) – see alternating protocols SAALT2W and SAALT3W**

TESTS:

- Baseline and before each treatment: CBC & diff, platelets, sodium, potassium, phosphate, albumin, bilirubin, creatinine
- If Day 1 CBC and diff or creatinine levels are ABNORMAL, recheck CBC and diff or creatinine on Day 4. Notify MD of Day 4 results prior to administering chemotherapy on Day 5.
- Urine dipstick for blood before each treatment and every 8 hours during treatment – if positive at any time, notify doctor and send urine sample for urinalysis for verification and accurate determination of hematuria. If hematuria verified (ie 50 RBC/hpf on urinalysis report), refer to supportive care protocol SCMESNA (follow SCMESNA (SAIME/SAAVIME3) pre-printed order)
- Imaging of primary site and any metastatic disease is done after three cycles.

PREMEDICATIONS:

- Antiemetic protocol for high-moderate emetogenic chemotherapy protocols (see SCNAUSEA)
- For etoposide reaction: hydrocortisone 100 mg IV and diphenhydrAMINE 50 mg IV as needed

TREATMENT:

Given daily for 5 consecutive days

- Repeat EVERY 3 WEEKS, for total of 7 cycles.
- **During radiation therapy (XRT) SAIME may be repeated**
- Filgrastim (G-CSF) to start Day 8 – if the treatment is potentially curative and after experience with one or more cycles of treatment indicate filgrastim (G-CSF) is required. (See Pharmacare guidelines).

Filgrastim may not be used to escalate doses beyond those specified in the protocol. The patient should be treated with filgrastim (G-CSF) in doses sufficient to allow full dose treatment on schedule using the dose modifications below.

Hour	Drug	Dose	BC Cancer Administration Guide
0	etoposide	100 mg/m ²	IV in 250 to 1000 mL NS over 45 min to 1 h 30 min (use non-DEHP equipment with 0.2 micron in-line filter)
1	mesna	360 mg/m ²	IV in 100 mL NS over 15 min
	followed by		
	ifosfamide*	1800 mg/m ²	IV in 500 mL NS over 1 h
2.25 –9	After completion of Ifosfamide infusion: <ul style="list-style-type: none"> • For patients receiving MESNA orally, no further hydration needed. • For patients receiving MESNA by IV, continue hydration with NS IV at 250 mL/h until after Hour 9 Mesna. 		
5 and 9	mesna**	360 mg/m ²	IV in 100 mL NS over 15 min
		720 mg/m ²	PO in carbonated beverage as outpatient
9	NS IV at 150 mL/h for 8 hours <ul style="list-style-type: none"> • For patients who are hydrating well and have not had hematuria, IV hydration may be discontinued daily after Hour 9 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 72 g/m² as there is an increased risk of Renal Fanconi Syndrome in children.

** If tolerated, may use oral mesna for last day of inpatient SAIME to allow for more timely discharge

DOSE MODIFICATIONS:

If dose reduced, stay at reduced dose level for the rest of program.

1. Hematological: for treatment day counts reduce **ALL** drugs

ANC (x10 ⁹ /L)		Platelets (x10 ⁹ /L)	Dose (ifosfamide, etoposide and mesna)
greater than or equal to 0.75	and	greater than or equal to 100	Give 100%
less than 0.75	or	less than 100	Delay for 1 week* If counts recover then give 100% If counts do NOT recover by Day 22 - then reduce doses by 20% and continue with Q 2 weekly dosing if possible

*If unable to give full dose after 1 week delay – use dose reduction as indicated or consult physician

- Nausea & Vomiting:** more than 10 episodes despite antiemetics and/or requiring parenteral fluid support, reduce dose of ALL DRUGS to 80%
- Hematuria:** See SCMESNA (follow SCMESNA (SAIME/SAAVIME3) pre-printed order)
- Renal Toxicity:** If serum creatinine increases greater than 100% or greater than twice institutional normal at any time during treatment (measured Days 1 and 4), estimate creatinine clearance using 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

- If creatinine clearance greater than 50 mL/min, continue with ifosfamide. If creatinine clearance less than 50 mL/min, discontinue course. If ifosfamide is discontinued midcycle, continue with MESNA for 48 hours.
 - If renal function does not return to normal by next cycle, GIVE ETOPOSIDE AS A SINGLE AGENT.
- CNS toxicity:** If drowsiness develops discontinue all sedating medications and continue ifosfamide. If patient is confused, unarousable or comatose, ifosfamide should be discontinued. 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 reinstated providing the previous medications contributing to CNS changes are not given with it. If a seizure occurs while on ifosfamide, then that cycle is to be discontinued. Further cycles may be given if the patient is on anticonvulsants.

7. **Etoposide hypotensive reaction:** Stop etoposide infusion. Lie patient flat and run NS IV. Give diphenhydrAMINE 25 to 50 mg IV and hydrocortisone 100 mg IV. Resume etoposide infusion in 20 to 30 minutes, once patient is stable. For subsequent doses of etoposide, pre-medicate with diphenhydrAMINE 25 to 50 mg IV and hydrocortisone 100 mg IV.

PRECAUTIONS:

1. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Hypersensitivity:** Monitor infusion of etoposide for the first 15 minutes for signs of hypotension. Refer to BC Cancer Hypersensitivity Guidelines.
3. **Venous access:** ensure good venous access prior to starting ifosfamide so that MESNA can be given at completion of ifosfamide.

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. Schuchter LM, Hensley ML, Meropol NJ, et al. 2002 Update of recommendations for the use of chemotherapy and radiotherapy protectants: clinical practice guidelines of the American Society of Clinical Oncology. *J Clin Oncol* 2002;20(12):2895-903.
2. Grier HE., Krailo MD, et al. Addition of ifosfamide and etoposide to standard chemotherapy for Ewing's sarcoma and primitive neuroectodermal tumor of bone. *N Engl J Med* 2003;348(8): 694-701.
3. Reaman G, Womer R, Krailo MD, Marina N. Memo: Chemotherapy for localized Ewing sarcoma: AEWS0031 results. In: Members C, editor. Arcadia, CA: COG; 2007. p. 1.