

BCCA Protocol Summary for Doxorubicin – Ifosfamide - Mesna For Use In Patients With Advanced Soft Tissue Sarcoma

Protocol Code	SAAI
Tumour Group	Sarcoma
Contact Physician	Dr. Meg Knowing

ELIGIBILITY:

- Patients with an advanced 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, lytes, calcium, albumin, creatinine, bilirubin, AST, alk phos, GGT, LDH and clinical measure of tumor response
- Urine dipstick for blood before each treatment as well as during treatment at hours 2, 16, 28 and 40 – if positive at any time, notify doctor and refer to supportive care protocol [SCMESNA](#)
- If clinically indicated: chest x-ray or other imaging to monitor response

PREMEDICATIONS:

- **Ondansetron** 8 mg PO/IV pre-chemotherapy, then 8 mg PO/IV q8h x 2 doses post-chemotherapy
- **Dexamethasone** 8 mg PO/IV pre-chemotherapy, then 4 mg PO/IV q12h x 2 doses post-chemotherapy
- **Lorazepam** 1 mg SL q 4-6 hr prn for nausea, sleep or restlessness
- **Prochlorperazine** 10 mg PO/IV q 4-6 hr prn for nausea or vomiting

TREATMENT:

Drug	Dose	BCCA Administration Guidelines
Doxorubicin	60 mg/m ²	IV push
Mesna	600 mg/m ²	IV in 100 mL D5W over 15 minutes
Ifosfamide	5000 mg/m ²	IV in 3 L of D5NS with Mesna 2500 mg/m ² to infuse over 24 hr. Total dose to be divided equally between three 1 L bags with each litre to be run over 8 hr.
Mesna	1250 mg/m ²	IV in 2 L of D5NS to infuse over 12 hr. Total dose to be divided equally between two 1 L bags with each litre to be run over 6 hr.
Furosemide	20 mg	IV at hour 16 and 28

Repeat every 21 days

DOSE MODIFICATIONS:**1. Hematological:**

ANC (x 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	Dose (all drugs)
greater than 1.5	and	greater than 100	100 %
1.0 – 1.5	or	70 – 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:

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

* 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/m² 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 10⁹/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
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 reinstated 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/m² to be exceeded. Refer to BCCA Cancer Drug Manual.
4. **Extravasation:** Doxorubicin causes pain and tissue necrosis if extravasated. Refer to BCCA Extravasation Guidelines.
5. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BCCA Febrile Neutropenia Guidelines.

Call Dr. Meg Knowling or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date Activated:

Date(s) Revised: 1 Feb 2010 (Tests clarified, furosemide added to Treatment section for diuresis)