BC Cancer Protocol Summary for Adjuvant Therapy for Rhabdomyosarcoma Using vinCRIStine, DACTINomycin, and Cyclophosphamide

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

ELIGIBILITY:

- Treatment of rhabdomyosarcoma[1,2] instead of SAVAC
- Treatment of sarcomas[3] where DOXOrubicin cumulative dose target has been reached using SAVAC
- Good performance status
- Adequate bone marrow, liver and kidney function

EXCLUSIONS:

- Pelvic primaries where bladder will receive radiotherapy

TESTS:

- Baseline and before each treatment: CBC & platelets, creatinine, bilirubin, ALT, Alk Phos, GGT, LDH and objective measure of tumour response

PREMEDICATIONS:

- Antiemetic protocol for high emetogenic chemotherapy protocols (see SCNAUSEA)

TREATMENT:

- Repeat every 6 weeks, alternating with SAIME every 3 weeks.
  - For young patients with Ewing's sarcoma, may repeat every 4 weeks, alternating with SAIME every 2 weeks.
- During radiotherapy:
  - Omit DACTINomycin (i.e., continue with vinCRIStine and cyclophosphamide according to this protocol, and alternating with SAIME
- After completion of radiotherapy:
  - Resume DACTINomycin, i.e., continue with SAVDC according to this protocol, and alternating with SAIME
- May be given as inpatient OR outpatient chemotherapy

Drug	Dose	BC Cancer Administration Guideline
vinCRIStine	1.5 mg/m² (maximum dose = 2 mg)	IV in 50 mL NS over 15 minutes
DACTINomycin	40 mcg/kg (maximum dose = 2.5 mg)	IV push
cyclophosphamide	1200 mg/m^2	IV in 500 mL D5½-NS over 1 hour

DOSE MODIFICATIONS:

1. **Hematological:** Adjust DACTINomycin and cyclophosphamide doses only

a. Pre-radiotherapy/pre-operative phase:

ANC (x10^9/L)		Platelets (x10^9/L)	Doses
greater than or equal to 0.5	and	greater than or equal to 100	100%
less than 0.5	or	less than 100	delay 1 week*

b. Radiotherapy phase:

ANC (x10^9/L)		Platelets (x10^9/L)	Doses
greater than or equal to 1.0	and	greater than or equal to 100	100%
less than 1.0	or	less than 100	delay 1 week*

c. Post-radiotherapy/post-operative phase:

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Doses
greater than or equal to 0.75	and	greater than or equal to 100	100%
less than 0.75	or	less than 100	delay 1 week*

*if counts remain low after 1 week delay, consult Dr. Simmons for further dose modifications.

2. **Neurotoxicity**: vinCRIStine only:

Toxicity	Dose Modification
Dysesthesias, areflexia only	100 %
Abnormal buttoning, writing	67%
Motor neuropathy, moderate	50%
Motor neuropathy, severe	omit

3. **Nausea & Vomiting:** If greater than 10 episodes of emesis post-chemotherapy despite optimal use of antiemetics and/or if parenteral fluid support is required, reduce dose of DACTINomycin and cyclophosphamide to 80%
4. **Hepatic dysfunction**: Dose modifications may be required for DACTINomycin and vinCRIStine (see BC Cancer Drug Manual)
5. **Renal dysfunction:** Dose modification may be required for cyclophosphamide (see BC Cancer Drug Manual).
6. **Neutropenic Fever** (with ANC less than 0.5 x 10^9/L): Once counts have recovered, either give 100% dosing with filgrastim coverage or reduce dose of DACTINomycin and cyclophosphamide to 80%
7. **Hematuria:** Call Dr. Simmons
8. **Severe Peripheral Neuropathy or Obstipation:** Discontinue vinCRIStine.

PRECAUTIONS:

1. **Extravasation:** DACTINomycin and vinCRIStine cause pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
2. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.

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

References:

1. Raney RB, Maurer HM, Anderson JR, et al. The Intergroup Rhabdomyosarcoma Study Group (IRSG): major lessons from the IRS-I through IRS-IV studies as background for the current IRS-V treatment protocols. Sarcoma 2001;5(1):9-15.
2. Arndt CA, Stoner JA, Hawkins DS, et al. vincristine, actinomycin, and cyclophosphamide compared with vincristine, actinomycin, and cyclophosphamide alternating with vincristine, topotecan, and cyclophosphamide for intermediate-risk rhabdomyosarcoma: Children's Oncology Group Study D9803. J Clin Oncol 2009;31(1):5182-8.
3.. Grier HE, Krailo MD, Tarbell NJ, 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.