BC Cancer Protocol Summary for Therapy for Soft Tissue Sarcomas using Gemcitabine and DOCEtaxel

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

ELIGIBILITY:

- First line treatment of leiomyosarcoma
- Second line treatment of soft tissue sarcoma following SAAI (ifosfamide and DOXOrubicin) or if either DOXOrubicin or ifosfamide is contraindicated or third line treatment following single agent ifosfamide as well as single agent DOXOrubicin
- To continue beyond 6 cycles, a BC Cancer "Compassionate Access Program" request must be approved.

TESTS:

- Baseline: CBC & Diff, platelets, total bilirubin, alkaline phosphatase, ALT, LDH, GGT, creatinine
- Before each treatment: CBC & Diff, platelets
- Before Cycle 4 and anytime if clinically indicated*: total bilirubin, alkaline phosphatase, ALT, LDH, GGT
- If clinically indicated at anytime: creatinine, total bilirubin, alkaline phosphatase, ALT, LDH, GGT, urea, total protein, albumin

  *See Precaution #7 for guidelines regarding hepatic dysfunction

PREMEDICATIONS:

- dexamethasone 8 mg PO bid for 3 days, starting on Day 7 (one day prior to each DOCEtaxel administration); patient must receive minimum of 3 doses pre-treatment
- prochlorperazine 10 mg PO or metoclopramide 10 mg PO prior to treatment as needed on Days 1 and 8
- ondansetron 8 mg PO on Day 8, 30 to 60 minutes prior to treatment
- DOCEtaxel-induced onycholysis and cutaneous toxicity of the hands may be prevented by wearing frozen gloves starting 15 minutes before DOCEtaxel infusion until 15 minutes after end of DOCEtaxel infusion; gloves should be changed after 45 minutes of wearing to ensure they remain cold during the entire DOCEtaxel infusion.

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
gemcitabine	900 mg/m^2 on Day 1 and Day 8 (for previously treated patients, consider starting at 750 mg/m^2 and escalate dose according to patient tolerance)	IV in 250 mL NS run at a rate of 10 mg/m^2/min (eg. 900 mg/m^2 should run over 1 hour 30 min)
DOCEtaxel	75 mg/m^2 on Day 8 only (for patients in excellent clinical condition especially if Filgrastim is available, may consider starting at 100 mg/m^2	IV in 250 to 500 mL NS over 1 hour (use non-DEHP equipment)

- Repeat every 21 days x 6 cycles

DOSE MODIFICATIONS:

1. Hematological

Day 1 Counts

ANC (x 10^9/L)		Platelets (x 10^9/L)	Percent of previous cycle Day 1 gemcitabine dose
greater than or equal to 0.9	and	greater than or equal to 100	100%
less than 0.9	or	less than100	Delay 1 week
• Grade 4 febrile neutropenia with previous cycle • greater than 2 week delay of the start of next cycle due to toxicity			75%*

***also dose reduce Day 8 DOCEtaxel to 75%**

Day 8 Counts

ANC (x 10^9/L)		Platelets (x 10^9/L)	Percent of previous cycle Day 8 DOCEtaxel	Percent of Day 1 gemcitabine
greater than or equal to 1.4	and	greater than or equal to 100	100%	100%
1.0 to less than 1.4	or	50 to less than 100	75%	100%
0.7 to less than 1.0	and	greater than or equal to 50	50%	100%*
less than 0.7	or	less than 50	Hold and reassess on Day 1 next cycle	

***gemcitabine may be dose reduced based upon clinical judgment of oncologist.**

2. Non-hematologic toxicity (except neurotoxicity, hepatotoxicity)

NCIC Grade	Percent of previous cycle Day 1 gemcitabine dose
0 to 2 (except nausea and vomiting or alopecia)	100%
3 (except nausea and vomiting or alopecia)	75% or hold (at discretion of treating physician)
4	50% or hold (at discretion of treating physician)

3. (i) Grade 2 Neurotoxicity – Symptomatic weakness, sensory alteration or paresthesia (including tingling) interfering with function, but not interfering with ADL

	Percent of previous cycle Day 8 DOCEtaxel dose
First occurrence	75%
If persistent on 75%	50%
If persistent on 50%	Hold therapy until symptoms less than or equal to grade 1 toxicity. Discontinue DOCEtaxel therapy if symptoms do not resolve within 6 weeks.

(ii) Grade 3 Neurotoxicity – Weakness, sensory alteration or paresthesia interfering with ADL; bracing or assistance to walk (e.g., cane or walker) indicated

	Percent of previous cycle Day 8 DOCEtaxel dose
Any occurrence	Hold DOCEtaxel therapy until symptoms less than or equal to grade 1 toxicity. Discontinue DOCEtaxel therapy if symptoms do not resolve within 6 weeks.
Recovery to grade less than or equal to 1	Reinstitute at 50% (Physician can escalate dose at their discretion)
No Recovery to grade less than or equal to 1	Discontinue DOCEtaxel

5. Hepatic Dysfunction

Alkaline Phosphatase		AST and/or ALT	DOCEtaxel Dose
less than 2.5 x ULN	and	less than or equal to 1.5 x ULN	100%
2.5 to 5 x ULN	and	1.6 to 5 x ULN	75%
greater than 5 x ULN	or	greater than 5 ULN	Discuss with contact physician

ULN = upper limit of normal

PRECAUTIONS:

1. **Renal Dysfunction**: Irreversible renal failure associated with hemolytic uremic syndrome may occur (rare). Use caution with pre-existing renal dysfunction.
2. **Pulmonary Toxicity**: Acute shortness of breath may occur. Discontinue treatment if drug-induced pneumonitis is suspected.
3. **DOCEtaxel Hypersensitivity**: Reactions are common but it is not necessary to routinely initiate the infusion slowly. If slow initiation of infusion is needed, start infusion at 30 mL/h x 5 minutes, then 60 mL/h x 5 minutes, then 120 mL/h x 5 minutes, then complete infusion at 250 mL/h (for 500 mL bag, continue 250 mL/h for 5 minutes and then complete infusion at 500 mL/h). Refer to BC Cancer Hypersensitivity Guidelines
4. **Fluid retention**: Dexamethasone premedication must be given to reduce incidence and severity of fluid retention.
5. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
6. **Extravasation**: DOCEtaxel causes pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
7. **Hepatic Dysfunction**: DOCEtaxel undergoes hepatic metabolism. Hepatic dysfunction (particularly elevated AST) may lead to increased toxicity and usually requires a dose reduction. Baseline liver enzymes are recommended before cycle 1 and then if clinically indicated (eg, repeat liver enzymes prior to each treatment if liver enzymes are elevated, liver metastases are present or there is severe toxicity such as neutropenia). If liver enzymes are normal and there is no evidence of liver metastases or severe toxicity, check liver enzymes after 3 cycles (ie, at cycle 4). Note: this information is intended to provide guidance but physicians must use their clinical judgment when making decisions regarding monitoring and dose adjustments

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. Maki RG, Wathen JK, Patel SR, et al. Randomized phase II study of gemcitabine and docetaxel compared with gemcitabine alone in patients with metastatic soft tissue sarcomas: results of sarcoma alliance for research through collaboration study 002 [corrected]. J Clin Oncol 2007;25(19):2755-63.
2. Cancer Therapy Evaluation Program, Common Terminology Criteria for Adverse Events, Version 3.0, DCTD, NCI, NIH, DHHS March 31, 2003 (http://ctep.cancer.gov), Publish Date: August 9, 2006. Accessed 05 Oct 2009.
3. Hensley ML. Update on gemcitabine and docetaxel combination therapy for primary and metastatic sarcomas. Curr Opin Oncol 2010;22(4):356-61.