BC Cancer Protocol Summary for Treatment of Uterine Sarcoma Cancer Using DOCEtaxel and Gemcitabine

Protocol Code	*GOSADG*
Tumour Group	*Gynecology*
Contact Physician	*Dr. Paul Hoskins*

ELIGIBILITY:

- Uterine sarcoma, advanced (residual disease) or recurrent or failed other chemotherapy
  - Leiomyosarcoma*
  - Endometrial stromal sarcoma*
  - Sarcoma NOS*
  - Malignant mixed mullerian (GOENDCAT recommended as first choice chemotherapy)

*Alternative possible treatments are (1) SAAI and (2) SAAVA (see sarcoma tumour group protocols). It is not known which alternative is superior so is physician choice between GOSADG, SAAI, SAAVA as first line choice.

EXCLUSIONS (RELATIVE):

- Warfarin (increased anticoagulation – monitor INR)
- Pneumonitis
- Liver impairment (Alk Phos greater than or equal to 5 x ULN, AST & ALT greater than or equal to 5 x ULN)
- PACLitaxel hypersensitivity
- Age greater than or equal to 80 years

TESTS:

- Baseline: CBC & diff, platelets, ALT, Alk Phos, creatinine. If clinically indicated: sodium, potassium, GGT, imaging.
- Before each treatment:
  - Day 1: CBC & diff, platelets; if abnormal at baseline: ALT, Alk Phos, creatinine.
  - Day 8 in Cycle 1 and in any Cycle when a dose adjustment has been made: CBC & diff, platelets.
- If clinically indicated: Tumour markers, imaging, protein, albumin, bilirubin, GGT, LDH, BUN.

PREMEDICATIONS:

- Dexamethasone 8mg PO bid x 6 doses, starting 24 hours prior to DOCEtaxel.
- Antiemetic protocol for low emetogenic chemotherapy protocols (see SCNAUSEA)
- 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
DOCEtaxel	80* mg/m^2 on Day 1	IV in 250 to 500 mL NS (non-DEHP bag) over 1 hour
gemcitabine	800* mg/m^2 on Day 1 and Day 8	IV in 250 mL NS over 30 minutes

* if greater than 80 years old or prior pelvic radiotherapy, start with 80% dosing. Can escalate to 100% in subsequent cycle if feasible.

Repeat every 21 days until progression or unacceptable toxicity. Discontinue if no response after 3 cycles.

DOSE MODIFICATIONS:

1. **Hematological (Day 1):**

ANC (x10^9/L)		Platelets (x10^9/L)	DOCEtaxel	Gemcitabine
greater than or equal to 1.0	and	greater than or equal to 100	100%	100%
less than 1.0	and/or	less than 100	delay	delay
upon recovery			80%	80%

NB - Dose may be increased at physician's discretion, 10% per cycle.

If monocytes greater than or equal to 20% of total WBC count and neutrophils greater than or equal to 0.8, then count recovery is likely imminent, and treatment can proceed at 100% dose, at physician's discretion.

Hematological (Day 8 – if applicable): hold Gemcitabine if ANC less than 0.5 and/or Platelets less than 100. For next cycle dosing, call Contact Physician.

2. **Hepatic dysfunction**: Dose modification required:

ALK PHOS	ALT	DOCEtaxel	Gemcitabine
less than 2.5 x ULN	less than 1.5 x ULN	100%	100%
2.6 to 5 x ULN	1.6 to 5 x ULN	75%	100%
greater than 5 x ULN	greater than 5 x ULN	Discuss with contact MD	

3. **Hemolytic Uremic Syndrome**: discontinue Gemcitabine.

4. **Peripheral Neuropathy**: if greater than or equal to Grade 2, reduce DOCEtaxel to 80% of previous dose.

5. **Pneumonitis**: discontinue Gemcitabine.

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
2. **Extravasation**: DOCEtaxel causes pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
3. **Hypersensitivity**: Reactions to DOCEtaxel 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. **Renal Toxicity**: Irreversible renal failure associated with Gemcitabine-induced hemolytic uremic syndrome may occur (rare). Use caution with pre-existing renal dysfunction.
5. **Pulmonary Toxicity**: Acute shortness of breath may occur. Discontinue Gemcitabine if drug-induced pneumonitis is suspected.
6. **Fluid retention**: Dexamethasone premedication must be given to reduce incidence and severity of fluid retention caused by DOCEtaxel.
7. **Hepatic Dysfunction**: DOCEtaxel undergoes hepatic metabolism. Hepatic dysfunction (particularly elevated AST) may lead to increased toxicity and usually requires a dose reduction (see table, above).

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

References:

1. Hensley, ML, Maki R, Venkatraman E, et al. J Gemcitabine and DOCEtaxel in patients with unresectable leiomyosarcoma: results of a phase II trial. J Clin Oncol 2002;20(12):2824-31.
2. 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. 2007;25(19):2755-63.