BC Cancer Protocol Summary for Palliative Therapy for Germ Cell Cancers Using PACLitaxel and Gemcitabine

Protocol Code	*GUTAXGEM*
Tumour Group	*Genitourinary*
Contact Physician	*Dr. Christian Kollmannsberger* *Dr. Bernie Eigl*

ELIGIBILITY:

- Relapsed germ cell cancers not amenable to cure with surgery or chemotherapy
- Cisplatin-refractory (failed during 1st-line EP/BEP or after 2nd-line VIP/VEIP)
- Patients relapsed after BMT are potentially eligible

EXCLUSIONS:

- PS 3-4
- Motor neuropathy
- ANC less than 1.5, Platelet less than 100, ALT or AST greater than 4xULN, bilirubin greater than 35, or creatinine greater than 180

TESTS:

- Baseline: CBC and differential, platelets, creatinine, ALT, alkaline phosphatase, bilirubin, LDH, AFP, beta hCG tumour marker
- Weekly during treatment: CBC and differential, platelets
- Prior to each cycle: creatinine, ALT, alkaline phosphatase, bilirubin, LDH, AFP, beta hCG tumour marker, monitor for neuropathy
- Relevant imaging for response every 8 weeks (baseline and alternate cycles)

PREMEDICATIONS:

- **PACLitaxel must not be started unless the following drugs have been given:**
  45 minutes prior to PACLitaxel:
  - dexamethasone 20 mg IV in 50 mL NS over 15 minutes

  30 minutes prior to PACLitaxel:
  - diphenhydrAMINE 50 mg IV in NS 50 mL over 15 minutes and famotidine 20 mg IV in NS 100 mL over 15 minutes (Y-site compatible)
- Additional antiemetics not usually required.

TREATMENT:

- Cycle length four weeks, repeat every 28 days x 2 - 6 cycles.
- Discontinue if no response after 2 cycles.

Drug	Dose	BC Cancer Administration Guideline
PACLitaxel	110 mg/m² (d1, 8, 15)	IV in 250 to 500 mL NS over 1 hour (use non-DEHP bag and non-DEHP tubing with 0.2 micron in-line filter)
gemcitabine	1,000 mg/m² (d1, 8, 15)	IV in 250 mL NS over 30 min

DOSE MODIFICATIONS:

1. **Hematological**

ANC (x10^9/L)		Platelets (x10^9/L)	Dose (both drugs)*
greater than or equal to 1.5	and	greater than or equal to 75	100% of previous cycle
1.0 to less than 1.5	and/or	50 to less than 75	75% of previous cycle
0.5 to less than 1.0	and/or	25 to less than 50	50% of previous cycle
less than 1.0	and/or	less than 25	Omit (d8) or delay (d1) **

*** a dose reduction for granulocytopenic fever or thrombocytopenia within a cycle results in a reduction of 25% in the start dose of the next cycle**

** if day 15, omit and start next cycle on day 22 instead of day 29

2. **Gastrointestinal Toxicities**

Grade	Stomatitis	Diarrhea	Dose Gemcitabine
1	Painless ulcers, erythema or mild soreness	Increase of 2-3 stools/day or mild increase in loose watery colostomy output	100%
2	Painful erythema, edema, or ulcers but can eat	Increase of 4-6 stools, or nocturnal stools or mild increase in loose watery colostomy output	Omit until toxicity resolved then resume at 100%
3	Painful erythema, edema, or ulcers and cannot eat	Increase of 7-9 stools/day or incontinence, malabsorption; or severe increase in loose watery colostomy output	Omit until toxicity resolved then resume at 75%
4	Mucosal necrosis, requires parenteral support	Increase of 10 or more stools/day or grossly bloody diarrhea, or grossly bloody colostomy output or loose watery colostomy output requiring parenteral l support; dehydration	Omit until toxicity resolved then resume at 50%.

3. **Other Non-Hemtological Toxicities**: dose modifications recommended for

- LFTs greater than or equal to 2 x ULN
- nausea Grade 4
- myalgia/rash Grade 3
- other toxicities of Grade 2-4 severity (excluding alopecia)

For more details, consult Table 2 of the referenced article.

PRECAUTIONS:

1. **Hypersensitivity**: Reactions are common with PACLitaxel. See BC Cancer Hypersensitivity Guidelines.
2. **Extravasation**: PACLitaxel causes pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
3. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
4. **Thrombocytopenia**: platelet support may be required as per local guidelines.
5. **Renal Dysfunction**: Irreversible renal failure associated with hemolytic uremic syndrome may occur with gemcitabine (rare). Use caution with pre-existing renal dysfunction.
6. **Pulmonary Toxicity**: Acute shortness of breath may occur. Discontinue treatment if gemcitabine-induced pneumonitis is suspected.
7. **Arthralgia and/or Myalgia**: if unrelieved by acetominophen ± codeine, try
   - Prednisone 10 mg po bid x 5 days starting 24 hours post-PACLitaxel
   - Gabapentin 300 mg po on day before chemotherapy, 300 mg bid on treatment day, then 300 mg tid x 7-10 days
8. **Neuropathy**: Dose modification or discontinuation may be required (see BC Cancer Drug Manual).

Contact Dr. Christian Kollmannsberger, Dr. Bernie Eigl or tumour group delegate at (604) 877-2730 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Reference:

1. Hinton S, Catalano P, Einhorn LH, et al. Phase II study of paclitaxel plus gemcitabine in refractory germ cell tumors (E9897): a trial of the Eastern Cooperative Oncology Group. J Clin Oncol 2002;20(7):1859-63 (Erratum in J Clin Oncol 2002;20(17):3754).