BC Cancer Protocol Summary for Advanced Therapy for Relapsed Testicular Germ Cell Cancer Using PACLitaxel, Ifosfamide and CISplatin (TIP)

Protocol Code	*GUTIP*
Tumour Group	*Genitourinary*
Contact Physician	*Dr. Kollmannsberger*

PATIENTS WITH RELAPSED TESTICULAR CANCER SHOULD BE REFERRED TO AN EXPERT CENTER AND DISCUSSED IN A MULTIDISCIPLINARY TUMOR BOARD

ELIGIBILITY:

- Relapsed Testicular Germ Cell Cancer
- Adequate renal function: Creatinine clearance greater than 60 mL/min
- Filgrastim (G-CSF) is not covered as a benefit at the BC Cancer

TESTS:

- Baseline: CBC & diff, platelets, creatinine, electrolytes panel, phosphate, albumin, bilirubin, LDH, AFP, beta hCG tumour marker, mental status, random glucose
- Before each treatment: CBC & diff, platelets, creatinine, electrolytes panel, phosphate, albumin, bilirubin, LDH, AFP, beta hCG tumour marker, mental status, random glucose
- If Day 1 CBC & diff, creatinine levels are abnormal, recheck CBC & diff, creatinine on Day 6. Notify MD of Day 6 results prior to administering chemotherapy on Day 6
- Dipstick urine for Blood prior to chemo on Day 2 and q 8 hours routinely. If positive, notify MD - see supportive care protocol – SCMESNA
- Routine vital signs q 8 hrs starting on Day 2.
- Daily weights -notify MD if weight gain greater than or equal to 4 kg)
- Record level of consciousness q 4 hr starting on Day 2 – notify MD of any changes

PREMEDICATIONS:

- Antiemetic protocol for highly emetogenic chemotherapy protocols (see SCNAUSEA)
- **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)

TREATMENT:

Repeat every 21 days x 4 cycles. Discontinue if no response after 2 cycles.

- **Day 1**:

Drug	Dose	BC Cancer Administration Guide
PACLitaxel	175 mg/m^2	IV in 250 to 500 ml NS (use non-DEHP bag) over 3 h Use non-DEHP tubing with 0.2 micron in-line filter

- **Day 2- 6**:

Hour	Drug	Dose	BC Cancer Administration Guide
0	CISplatin	20 mg/m²	IV in 100 mL NS over 30 min
0.5	Mesna	300 mg/m²	IV in 100 mL D5W over 15 min
0.75	Ifosfamide	1200 mg/m^2	IV in 500 mL D5 ½ NS over 1 h
1.75 – 9	After completion of Ifosfamide infusion: • For patients receiving MESNA by IV, continue hydration with D5 ½ NS IV at 250 mL/h until after Hour 9 Mesna.		
5 and 9	Mesna	300 mg/m²	IV in 100 mL D5W over 15 min
9	Either: ☐ Continue D5 ½ NS IV at 150 mL/hr x 8 hours • ONLY patients with hematuria requiring Mesna dose adjustments are required to be treated on a 24 hour schedule. OR: ☐ Discontinue IV fluids and cap access - patient able to take at least 1 litre of fluids over 8 hours and not had hematuria • For patients who are hydrating well and have not had hematuria, IV hydration may be discontinued daily after Hour 9 Mesna bolus. OR: ☐ Allow out on pass		

- **Day 9:**

Start Filgrastim (G-CSF) for 5-7 days (until neutrophil recovery)

DOSE MODIFICATIONS:

This program is given with curative intent. Any delay or dose reduction may have serious implications and can result in inferior outcomes. Treat with filgrastim (G-CSF) in doses sufficient to allow full dose treatment on schedule. Refer to Pharmacare guidelines.

1. Hematological:

For cycles of PACLitaxel:

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose (PACLitaxel)
greater than or equal to 1.0	and	greater than 90	175 mg/m^2
less than 1.0	or	less than 90	delay

For cycles of Ifosfamide:

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose (Ifosfamide)
greater than or equal to 1.0	and	greater than or equal to 75	Give 100%
less than 1.0	or	less than 75	Delay for 1 week

Dose reductions should only be implemented, if no recovery after a 1-week break. Dose reduction to 75% (or 50% in severe cases) for Ifosfamide and PACLitaxel can be considered. CISplatin should only be dose reduced for renal failure.

2. Renal dysfunction: For CISplatin and ifosfamide

Serum creatinine greater than 150 micromol/L:	Prehydrate
Serum creatinine greater than 200 micromol/L:	Prehydrate Reduce ifosfamide by 25%
Serum creatinine greater than 300 micromol/L:	Reduce CISplatin by 25% Reduce ifosfamide by 33%
Neutropenic fever:	Filgrastim (G-CSF) may be used for febrile neutropenia. Refer to Pharmacare guidelines.

3. **Hepatic dysfunction**: Dose modification required for PACLitaxel. Refer to BC Cancer Drug Manual.
4. **Arthralgia and/or myalgia**: If arthralgia and/or myalgia from PACLitaxel of grade 2 (moderate) or higher is not relieved by adequate doses of NSAIDS or acetaminophen with codeine (TYLENOL #3®) a limited number of studies report a possible therapeutic benefit from the following:
    - predniSONE 10 mg PO BID x 5 days starting 24 hours post PACLitaxel

- gabapentin 300 mg PO on day prior to PACLitaxel, 300 mg PO BID on treatment day and then 300 mg PO TID x 7-10 days

5. **Neuropathy**: Dose modification or discontinuation for PACLitaxel may be required. Refer to BC Cancer Drug Manual

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
2. **Hypersensitivity**: Reactions are common with PACLitaxel. Refer to BC Cancer Hypersensitivity Guidelines.

Mild symptoms (e.g. mild flushing, rash, pruritis)	▪ Complete PACLitaxel infusion. Supervise at bedside ▪ No treatment required
moderate symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension	▪ Stop PACLitaxel infusion ▪ Give IV DiphenhydrAMINE 25-50 mg and Hydrocortisone IV 100 mg ▪ After recovery of symptoms resume PACLitaxel infusion at 20 mL/h for 5 minutes, 30 mL/h for 5 minutes, 40 mL/h for 5 minutes, then 60 mL/h for 5 minutes. If no reaction, increase to full rate. ▪ If reaction recurs, discontinue PACLitaxel therapy
severe symptoms (i.e. *one* or more of respiratory distress requiring treatment, generalised urticaria, angioedema, hypotension requiring therapy)	▪ Stop PACLitaxel infusion ▪ Give IV antihistamine and steroid as above. Add Epinephrine or bronchodilators if indicated ▪ Discontinue PACLitaxel therapy

3. **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside

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

References:

1. Motzer RJ, Sheinfeld J, Mazumbar M, et al. Paclitaxel, ifosfamide and cisplatin second-line therapy for patients with relapsed testicular germ cell cancer. J Clin Oncol 2000;18(12):2413-8.
2. Mardiak J, Rejlekova M, Mego J, et al. Determination of efficacy of TIP combination (paclitaxel, ifosfamide, cisplatin) as first salvage therapy for patients with relapsed germ cell tumours in a poor prognosis group. J Clin Oncol 2009;27(15S);abstr e16049.