

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, sodium, potassium, phosphate, albumin, bilirubin, AFP, serum hCG, mental status, random glucose
- Before each treatment: CBC & diff, platelets, creatinine, sodium, potassium, phosphate, albumin, bilirubin, AFP, serum hCG, 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 and Ranitidine 50 mg IV in 50 mL NS over 20 minutes (compatible up to 3 hours when mixed in bag)

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 500 ml NS (use non-DEHP bag) over 3 h Use non-DEHP tubing with in-line filter

- **Day 2- 6:**

Hour	Drug	Dose	BC Cancer Administration Guide
0	CISplatin	20 mg/m ²	IV in 100 mL NS over 30 min
0.5	Mesna	300 mg/m ²	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: <ul style="list-style-type: none"> • 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/m ²	IV in 100 mL D5W over 15 min
9	Either: <ul style="list-style-type: none"> <input type="checkbox"/> Continue D5 ½ NS IV at 150 mL/hr x 8 hours <ul style="list-style-type: none"> • ONLY patients with hematuria requiring Mesna dose adjustments are required to be treated on a 24 hour schedule. OR: <ul style="list-style-type: none"> <input type="checkbox"/> Discontinue IV fluids and cap access - patient able to take at least 1 litre of fluids over 8 hours and not had hematuria <ul style="list-style-type: none"> • For patients who are hydrating well and have not had hematuria, IV hydration may be discontinued daily after Hour 9 Mesna bolus. OR: <ul style="list-style-type: none"> <input type="checkbox"/> 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.

<i>Mild</i> symptoms (e.g. mild flushing, rash, pruritis)	<ul style="list-style-type: none"> ▪ Complete PACLitaxel infusion. Supervise at bedside ▪ No treatment required
<i>moderate</i> symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension)	<ul style="list-style-type: none"> ▪ 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
<i>severe</i> symptoms (i.e. <u>one</u> or more of respiratory distress requiring treatment, generalised urticaria, angioedema, hypotension requiring therapy)	<ul style="list-style-type: none"> ▪ 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.