BC Cancer Protocol Summary for Etoposide-CISplatin Protocol for Germ Cell Cancers

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

ELIGIBILITY:

- Good prognosis seminoma or nonseminoma (international consensus prognostic [Cambridge] classification) if there are contraindications for GUBEP
- AFP less than 1000 mcg/L and serum beta hCG less than 5000 unit/L and LDH less than 1.5 times normal
- or pure seminoma

EXCLUSIONS:

- Mediastinal primary nonseminoma
- Intermediate or poor prognosis testicular cancer according to the IGCCCG classification
- Inadequate renal function (calculated creatinine clearance less than 40 mL/min) (relative contraindication)
- Inadequate hematologic function

It is strongly recommended that all patients with metastatic germ cell tumours should be presented in GU tumour group conference.

TESTS:

- *Baseline*: CBC and differential, platelets, bilirubin, ALT, alkaline phosphatase, LDH, creatinine, sodium, potassium, magnesium, calcium, AFP, beta hCG tumour marker, random glucose
- Consider baseline audiogram for pretreatment hearing impairment.
- Consider prechemotherapy sperm count and banking if fertility is an issue.
- *Before each cycle*: CBC and differential, platelets, creatinine, LDH, AFP, beta hCG tumour marker, magnesium, sodium, potassium, random glucose
- Repeat CBC on day 5 if ANC on day 1 less than 1.0 x 10^9/L (not required on day 5 of the first cycle)
- Repeat creatinine on day 5 if creatinine on day 1 greater than the upper limit of normal
- Repeat abnormal tests every 21 days (scans optional if markers responding appropriately)

PREMEDICATIONS:

- Antiemetic protocol for highly emetogenic chemotherapy protocols (see SCNAUSEA).
- hydrocortisone and diphenhydrAMINE for history of hypersensitivity to etoposide or etoposide phosphate (ETOPOPHOS)

TREATMENT:

- **Cycle length 21 Days regardless of ANC**
- **Duration: 4 cycles (3 cycles if adjuvant)**

Agent	Dose	BC Cancer Administration Standard	Duration
Pre-Hydration		IV 1000 mL NS with 20 mEq potassium chloride and 2 g magnesium sulfate over 1 hour	days 1 to 5
etoposide	100 mg/m²/day	IV in 250 to 1000 mL NS over 45 minutes to 1 hour 30 minutes (use non-DEHP equipment with 0.2 micron in-line filter)	days 1 to 5
CISplatin	20 mg/m²/day	IV in 100 mL NS over 30 minutes	days 1 to 5
Post-Hydration		IV 500 mL NS over 30 minutes	days 1 to 5
Total hydration:		IV 2100 mL NS	

NOTE: Treatment should be given on 5 consecutive days.

DOSE MODIFICATIONS:

- No dose reduction or delay is permitted for counts.
- This program is given with curative intent and any delay or dose reduction may have serious implications. In the event of elevated creatinine (e.g. greater than 200 micromol/L), neutropenic fever or low platelets, phone consultation with a contact physician is recommended.
- Prophylactic use of filgrastim is not recommended.
- Filgrastim is indicated in patients receiving their second or subsequent cycle of GUEP who have had an episode of neutropenic fever or who have not recovered their neutrophil count by Day 5.

Hypersensitivity: etoposide only:

When etoposide cannot be used due to severe hypersensitivity reaction to etoposide, it can be replaced by etoposide phosphate (ETOPOPHOS) as shown, below. Approval from the Health Canada Special Access Program must be obtained for each patient.

Agent	Dose	BC Cancer Administration Guideline	Duration
etoposide phosphate (ETOPOPHOS)	100 mg/m²/day	IV in 500 mL NS over 45 min to 1 hour 30 min	days 1 to 5

PRECAUTIONS:

1. **Hypersensitivity:** Monitor infusion of etoposide for the first 15 minutes for signs of hypotension. Hypersensitivity reactions have also been reported for CISplatin. Refer to BC Cancer Hypersensitivity Guidelines. Etoposide phosphate (ETOPOPHOS): Allergic reactions may be less common and severe than etoposide because etoposide phosphate does not contain polysorbate 80. Etoposide phosphate has been safely administered in patients with previous hypersensitivity although rare cross-sensitivity has been reported.
2. **Extravasation**: Etoposide and etoposide phosphate (ETOPOPHOS) cause irritation if extravasated. Refer to BC Cancer Extravasation Guidelines.
3. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
4. **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Strongly encourage oral hydration. If oral hydration is not possible (e.g. excessive nausea), IV hydration is indicated. Avoid nephrotoxic drugs such as aminoglycoside antibiotics.

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.

References:

1. International germ cell consensus collaborative group. International germ cell consensus classification: a prognostic factor-based staging system for metastatic germ cell cancers. J Clin Oncol 15:564-603, 1997
2. Einhorn LH, Williams SD, Loehrer PJ, et al. Evaluation of optimal duration of chemotherapy in favorable-prognosis disseminated germ cell tumors: a Southeastern Cancer Study Group protocol. J Clin Oncol 1989;7:387-91.
3. de Wit R, Roberts JT, Wilkinson P, et al. Final analysis demonstrating the equivalence of 3 BEP vs 4 cycles and the 5 day schedule vs 3 days per cycle in good prognosis germ cell cancer. An EORTC/MRC phase III study. Proc Am Soc Clin Oncol 2000;19a:326a (abstract 1281).
4. Siderov J, Prasad P, De Boer R, et al. Safe administration of etoposide phosphate after hypersensitivity reaction to intravenous etoposide. Br J Cancer. 2002 Jan 7;86(1):12-3.
5. Collier K, Schink C, Young AM, et al. Successful treatment with etoposide phosphate in patients with previous etoposide hypersensitivity. J Oncol Pharm Pract. 2008 Mar;14(1):51-5.