BC Cancer Protocol Summary for Therapy of Genitourinary Small Cell Tumors with a Platin and Etoposide with Radiation

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

ELIGIBILITY:
- Small cell cancer of the bladder (limited and extensive stage)
- Small cell cancer of the prostate (limited and extensive stage)
- Selected poorly differentiated prostate cancers demonstrating virulent behaviour (Hormone insensitive with low or modest PSA level)
- High-grade neuroendocrine tumours of the GU system.

EXCLUSIONS:
- Germ cell tumours (see GU protocols for testicular cancer)

TESTS:
- Baseline: CBC & differential, platelets, creatinine, bilirubin, ALT, alk phos, albumin, INR
- Before each cycle: CBC, differential, platelets, creatinine
- If clinically indicated: bilirubin

PREMEDICATIONS:
- Antiemetic protocol for High Moderate emetogenic chemotherapy protocols as long as CISplatin dose is not greater than or equal to 50 mg. If CISplatin is greater than or equal to 50 mg use antiemetic protocol for highly emetogenic chemotherapy protocols.
- If past etoposide drug reactions:
  - hydrocortisone 100 mg IV prior to etoposide
  - diphenhydrAMINE 50 mg IV prior to etoposide

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
CISplatin	25 mg/m^2/day x 3 days (days 1 to 3)	IV in **100 to 250 mL*** NS over 30 min
etoposide	100 mg/m^2/day x 3 days (days 1 to 3)	IV in 250 to 1000 mL NS over 45 min to 1 hour 30 min (use non-DEHP equipment with 0.2 micron in-line filter)
***If CISplatin dose less than or equal to 60 mg use 100 mL NS, if CISplatin dose greater than 60 mg use 250 mL NS**		

In cases of CISplatin toxicity or poorly functioning patients or Age greater than 75:

DRUG	DOSE	BC Cancer Administration Guidelines
CARBOplatin	AUC 5 DAY 1 only Dose = AUC x (GFR* +25)	IV in 100 to 250 mL NS over 30 minutes.

*Measured GFR (e.g. nuclear renogram) is preferred whenever feasible, *particularly* in circumstances of co-morbidity that could affect renal function (third-space fluid accumulations, hypoproteinemia, potentially inadequate fluid intake, etc.). The lab reported GFR (MDRD formula) may be used as an alternative to the Cockcroft-Gault estimate of GFR; the estimated GFR reported by the lab or calculated using the Cockcroft-Gault equation should be capped at 125 mL/min when it is used to calculate the initial carboplatin dose. When a nuclear renogram is available, this clearance would take precedence.

Cockcroft-Gault Formula

$$GFR = \frac{N^* \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}}$$

*For males in = 1.23; for females N = 1.04

Note: The *same* method of estimation should be used throughout the treatment course (i.e. if lab reported GFR was used initially, this should be used for dosing in all subsequent cycles and not the Cockcroft-Gault estimate).

- **Repeat every 21 days x 4 cycles except during concurrent radiotherapy (see below)**
- Radiation Therapy may be given concurrently with this protocol
- For patients with limited stage small cell carcinoma of the bladder or prostate (all macroscopic tumour encompassable within a reasonable radiotherapy volume and metastatic disease excluded by appropriate staging investigations) the radiotherapy should be given concurrently with the first or second chemotherapy cycle.
- For limited stage small cell carcinoma of the bladder or prostate patients treated with curative intent, the radiotherapy dose should consistent with this objective.
- For chemotherapy cycles given concurrently with pelvic irradiation, the appropriate interval between cycles is four weeks rather than three weeks with reduction to three weeks when the radiotherapy is complete.

DOSE MODIFICATIONS:

1. **Hematology:** for etoposide

ANC (X 10^9/L)		Platelets (x 10^9/L)	Dose
greater than or equal to 1.5	and	greater than or equal to 100	100%
1.0 to less than 1.5	or	75 to less than 100	75%
less than 1.0	or	less than 75	**Delay**

2. **Hepatic dysfunction:** for etoposide

Bilirubin (micromol/L)	**Dose**	
less than 25	100%	100 mg/m^2/day x 3 days
25 to 50	50%	50 mg/m^2/day x 3 days
51 to 85	25%	25 mg/m^2/day x 3 days
greater than 85	**Delay**	

3. **Renal dysfunction:** for CISplatin

Calculated Cr Clearance (mL/min)	**Dose**	
greater than or equal to 60	100%	25 mg/m^2/day x 3 days
45 to less than 60	60%	15 mg/m^2/day x 3 days
less than 45	**Delay**	

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.
2. **Extravasation**: etoposide causes 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. Encourage oral hydration. 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. Evans WK, Shepherd FA, Feld R, et al. VP-16 and cisplatin as first-line therapy for small-cell lung cancer. J Clin Oncol 1985;3(11):1471-7.
2. Boni C, Cocconi G, Bisagni G, et al. Cisplatin and etoposide (VP-16) as a single regimen for small cell lung cancer. A phase II trial. Cancer 1989;63(4):638-42.
3. Okamoto H, Watanabe K, Nishiwaki Y, et al. Phase II Study of Area Under the Plasma-Concentration-Versus-Time Curve-Based Carboplatin Plus Standard-Dose Intravenous Etoposide in Elderly Patients With Small-Cell Lung Cancer. J Clin Oncol 1999;17(11):3540-5.
4. Lohrisch C, Murray N, Pickles T, Sullivan L. Small cell cancer of the bladder: Long-term outcome with integrated chemoradiation. Cancer 1999;86:2346-52.