BC Cancer Protocol Summary for Palliative Therapy of Neuroendocrine Tumours using CISplatin and Etoposide

Protocol Code	*GIPE*
Tumour Group	*Gastrointestinal*
Contact Physician	*GI Systemic Therapy*

ELIGIBILITY:

Patients must have:

- Poorly differentiated, neuroendocrine carcinoma

Patients should have:

- ECOG 0 to 2
- Adequate marrow reserve, renal and liver function

TESTS:

- Baseline: CBC & Diff, creatinine, ALT, alkaline phosphatase, total bilirubin, albumin, sodium, potassium
- Baseline if clinically indicated: GGT, ECG
- Prior to each cycle: CBC & Diff, creatinine, total bilirubin, ALT
- If clinically indicated: alkaline phosphatase, albumin, GGT, sodium, potassium, ECG
- For patients on warfarin, weekly INR during treatment until stable warfarin dose established, then INR prior to each cycle

PREMEDICATIONS:

- Antiemetic protocol for moderately emetogenic chemotherapy as long as CISplatin dose is not greater than or equal to 50 mg. If CISplatin is greater than or equal to 50 mg, or if giving CARBOplatin, use antiemetic protocol for highly emetogenic chemotherapy. See SCNAUSEA.
- hydrocortisone & diphenhydrAMINE for history of hypersensitivity 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 minutes
etoposide	100 mg/m^2/day x 3 days (Days 1 to 3)	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)

In cases of CISplatin toxicity or poor performance status patients or Age greater than 75 CARBOplatin may be substituted for CISplatin

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.

*GFR use:

$$GFR = \frac{N \times (140\text{-age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}} \qquad N = 1.04 \text{ (women) or } 1.23 \text{ (men)}$$

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.

- Repeat every 21 days until disease progression or unacceptable toxicity (may extend to every 28 days if needed for recovery of cytopenias).

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 Creatinine Clearance (mL/min)	Dose
Greater than or equal to 60	100%
45 to less than 60	80% CISplatin or go to CARBOplatin option
Less than 45	Hold CISplatin or delay with additional IV fluids or go to CARBOplatin option

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 SCDRUGRX protocol.
2. **Extravasation**: Etoposide causes irritation if extravasated. Refer to BC Cancer Extravasation Guidelines – Systemic Therapy Policy III-20.
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.

Call the GI Systemic Therapy physician at your regional cancer centre or GI Systemic Therapy Chair Dr. Theresa Chan at (604) 930-2098 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):1471-1477.
2. Mitry E, et al. Treatment of poorly differentiated neuroendocrine tumours with Etoposide and Cisplatin. BJOC 1999 ; 81(8) :1351-1355.
3. Fjallskog, M-LH, et al. Treatment with Cisplatin and Etoposide in Patients with Neuroendocrine Tumors. Cancer 2001 ; 92(5) :1101-1107.
4. 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):3540-3545.