

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:

- Poorly differentiated, neuroendocrine carcinoma
- ECOG Performance Status 0-2
- Adequate marrow reserve (ANC greater than or equal to $1.5 \times 10^9/L$, platelets greater than $100 \times 10^9/L$)
- Adequate renal (Creatinine less than or equal to $1.5 \times ULN$) and liver function (bilirubin less than or equal to 26 micromol/L ; ALT/ Alkaline Phosphatase less than or equal to $5 \times ULN$)

TESTS:

- **Baseline:** CBC & differential, platelets, creatinine, LFTs (Bilirubin, ALT, Alkaline Phosphatase)
- **Prior to each cycle:** CBC, differential, platelets, creatinine
- If clinically indicated: bilirubin

PREMEDICATIONS:

- Antiemetic protocol for High Moderate 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 use antiemetic protocol for Highly emetogenic chemotherapy. See SCNAUSEA protocol.
- 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 1-3)	IV in 100 to 250 mL* NS over 30 min
etoposide	100 mg/m ² /day x 3 days (days 1-3)	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 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:

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

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 x 4-6 cycles (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
25-50	50%	50 mg/m ² /day x 3 days
51-85	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%
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 – Systemic Therapy Policy IV-10.
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. Janine Davies at (604) 877-6000 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):1471-1477.
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.