BC Cancer Protocol Summary for Treatment of recurrent or metastatic Merkel cell carcinoma (MCC) with CISplatin and Etoposide

Protocol Code	*SMMCCPE*
Tumour Group	*Skin and Melanoma*
Contact Physician	*Dr. Christopher Lee*

ELIGIBILITY:

Patients must have:
- Recurrent or metastatic Merkel cell carcinoma

EXCLUSIONS:

Patients must not have:
- History of hypersensitivity reaction to cisplatin or other platinum-containing compounds

CAUTIONS:

- Pre-existing renal impairment, myelosuppression or hearing impairment

TESTS:
- Baseline: CBC & Diff, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH
- Before each cycle: CBC & Diff,creatinine
- If clinically indicated: total bilirubin

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 using CARBOplatin, use antiemetic protocol for highly emetogenic chemotherapy (see protocol SCNAUSEA)
- hydrocortisone & diphenhydrAMINE for history of hypersensitivity to etoposide

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
(Drugs can be given in any sequence)		
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 poorly functioning patients or age greater than 75:

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

*GFR preferably from nuclear renogram, if not possible use:

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

The estimated GFR 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.

- **Repeat every 21 days x 4 to 6 cycles**

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	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 (if available)
less than 45	Hold CISplatin or delay with additional IV fluids or go to CARBOplatin option (if available)

For etoposide

Initial dose modification to 75% should be considered if creatinine clearance is less than 30 mL/min. Subsequent dosing should be based on patient tolerance and clinical effect.

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 SCDRUGRX.
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. Christopher Lee or tumour group delegate at 604-930-2098 or 1-800-523-2885 with any problems or questions regarding this treatment program.

References:

1. Goessling W, et al. Merkel cell carcinoma. J Clin Oncol 2002;20:588-98.
2. Allen PJ, et al. Merkel cell carcinoma: prognosis and treatment of patients from a single institution. J Clin Oncol 2005;23:2300-9.
3. Miller SJ, et al. Merkel cell carcinoma clinical practice guidelines in oncology. J Natl Compr Canc Netw 2014;7:322-32.