BCCA Protocol Summary for Adjuvant Lomustine, CISplatin and vinCRIStine in Adult High-Risk Medulloblastoma or other Primitive Neuro-Ectodermal Tumour (PNET)

Protocol Code *CNCCV*

Tumour Group *Neuro-Oncology*

Contact Physician *Dr. Brian Thiessen*

ELIGIBILITY:

- Adults greater than 18 yrs and less than or equal to 40 yrs with high risk medulloblastoma or supratentorial PNET (including pinealoblastoma)
- "High Risk" includes:
    1. residual tumour greater than 1.5 cm
    2. evidence of metastatic spread on neuroimaging and/or CSF analysis
    3. brainstem invasion by tumour

EXCLUSIONS:

- Patients greater than 40 yrs (consider for modified PCV adjuvant chemotherapy [CNMODPCV])
- Karnofsky Performance Score less than 60
- Significant hematologic, renal or liver dysfunction

TESTS:

- Baseline: CBC and diff, lytes, calcium, magnesium, creatinine, creatinine clearance (calculated using the formula below), AST, GGT, bilirubin, audiometric evaluation

$$\text{Creatinine clearance} = \frac{N^* \times (140 - \text{Age}) \times \text{Weight (kg)}}{\text{Serum creatinine}}$$

For males N= 1.23; For females N=1.04

- Before each cycle: CBC and diff, platelets, lytes, calcium, magnesium, creatinine, creatinine clearance (calculated), AST, GGT, bilirubin
- Before each treatment: CBC and diff, platelets
- Audiometry: After cycles 2, 4, 6,
- Neuroimaging: CT/MRI of head before cycles 3, 5, 7 and at the end of treatment, MRI spine at treatment completion
- If clinically indicated: Pulmonary function tests, more frequent audiometry

PREMEDICATIONS:

- Antiemetic protocol for highly emetogenic chemotherapy protocols (see protocol SCNAUSEA).

TREATMENT:

- 8 cycles of Lomustine, CISplatin and vinCRIStine administered every 6 weeks, starting 4 to 6 weeks after craniospinal RT:

Drug	Dose	BCCA Administration Guidelines
Prehydration	1000 mL D5 ½ NS	IV infusion from Hours 0 to 2
Lomustine	75 mg/m² on Day 1	PO (after prehydration)
CISplatin	75 mg/m² on Day 1	IV infusion in 1000 mL D5 ½ NS over 6 hours from Hours 2 to 8
Mannitol	30 g on Day 1	
Posthydration	D5 ½ NS	IV infusion at 200 mL/h from Hours 8 to 24
vinCRIStine	2 mg on Days 1, 8 and 15	in 50 mL NS over 5 mins

Repeat every 6 weeks x 8 cycles.

Discontinue if no response, progression, recurrence or completion of 8 cycles.

DOSE MODIFICATIONS:

1. **Hematological:** For treatment day counts, modify lomustine as follows,

ANC ($x10^9$/L)	Platelets ($x10^9$/L)	Dose (lomustine)
greater than or equal to 1.5	greater than or equal to 100	100%
1 to 1.5	80 to 100	80%
less than 1	less than 80	Delay and reinstitute at 60%

2. Renal dysfunction: Dose modification required for CISplatin,

Creatinine clearance (mL/min)	Dose (CISplatin)
greater than or equal to 60	100%
45 to 60	75% (same prehydration as 75 mg/m² dose)
less than 45	Delay until creatinine clearance greater than 45 mL/min, then give 50% of CISplatin dose*

*may reinstitute full dose CISplatin if renal function stable or improving after 2 more cycles

3. Ototoxicity: Dose modifications required for CISplatin,

Ototoxicity	Dose (CISplatin)
less than Grade 3	100%
Grade 3	50%
Grade 4	Hold unless audiograms show improvement

4. Hepatic dysfunction: Liver toxicity is idiosyncratic and usually reversible. Hold chemotherapy if AST/GGT greater than 5 x ULN or bilirubin greater than 25 micromol/L until liver function returns to normal.

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Extravasation**: vinCRIStine causes pain and tissue necrosis if extravasated. Refer to BCCA Extravasation Guidelines.
3. **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside.
4. **Neurotoxicity:** vinCRIStine commonly causes paresthesias, jaw pain and constipation. Hold for disabling motor neuropathy and reinstitute at 1.5 mg. CISplatin rarely causes sensory neuropathy with this dose schedule. Stop only for disabling sensory neuropathy.
5. **Nausea/vomiting:** Both CISplatin and lomustine are emetogenic. Antinauseants should be prescribed preemptively (see Premedications above).
6. **Hypomagnesemia:** Common with CISplatin. Refer to BCCA Cancer Drug Manual.
7. **Drug interaction with anticonvulsant:** CISplatin can decrease serum phenytoin levels. Refer to BCCA Cancer Drug Manual.

Call Dr. Brian Thiessen or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated: 01 Nov 1999 (replaced CNVCD2)

Date revised: 1 Mar 2013 (TALLman lettering)

References:

1. Packer RJ, Sutton LN, et al. Outcome for children with medulloblastoma treated with radiation and cisplatin, CCNU, and vincristine chemotherapy. J Neurosurg 1994;81:690-8.