BC Cancer Protocol Summary For Modified PCV Chemotherapy Of Brain Tumours Using Procarbazine, Lomustine (CCNU) and vinCRIStine

Protocol Code	*CNMODPCV*
Tumour Group	*Neuro-oncology*
Contact Physician	*Dr. Rebecca Harrison*

ELIGIBILITY:

Patients must have:

- Malignant gliomas*, or
- Embryonal tumours (adjuvant therapy for adults over age 40), such as medulloblastoma and other primitive neuroectodermal tumours

* Patients can use CNAJTZRT if they are ineligible for or intolerant of CNMODPCV, or have poor performance status

Patients should have:

- Adequate hematological, renal and hepatic function

TESTS:

- Baseline: CBC & Diff, creatinine, ALT, total bilirubin, random glucose (for patients on dexamethasone), anticonvulsant levels
- Before each cycle: CBC and diff, platelets, creatinine, ALT, total bilirubin, random glucose (for patients on dexamethasone)
- Day 22: CBC and diff, platelets (results not required to proceed with vinCRIStine)
  - CBC & Diff, ALT, total bilirubin, creatinine **before** last cycle.
- Imaging: CT or MR every 2nd cycle

PREMEDICATIONS

- ondansetron PO 8 mg q12h for 36 hours (starting 30 min before lomustine), then prochlorperazine PO or dimenhyDRINATE PO prn
- dexamethasone PO 8 mg q12h for 36 hours (starting 30 min before lomustine), then prochlorperazine PO or dimenhyDRINATE PO prn
- if patients are nauseated with procarbazine, may divide procarbazine dose or add regular prochlorperazine

TREATMENT:

Day	Drug	Dose	BC Cancer Administration Guideline
1	vinCRIStine	1.4 mg/m² (maximum 2mg)	IV in 50 mL NS over 15 mins
1	lomustine (CCNU)	110 mg/m² at bedtime	PO
2	procarbazine	60 mg/m²/day, days 2 to 15	PO
22	vinCRIStine	1.4 mg/m² (maximum 2mg)	IV in 50 mL NS over 15 mins (Day 22 counts not required to proceed with vinCRIStine)

- Adjuvant chemotherapy for primitive neuroectodermal tumour (PNET):
  - Repeat every 6 weeks x **4 to 6** cycles as tolerated
- Recurrent oligodendrogliomas and mixed gliomas not previously exposed to PCV or with a prior good response to PCV
  - Repeat every 6 weeks x **4 to 6** cycles based on response and tolerability
- Low grade gliomas, to start two weeks post radiation therapy
  - Repeat every 6 weeks x **6** cycles as tolerated

DOSE MODIFICATIONS:

1. **Hematological:** modify lomustine and procarbazine, not vinCRIStine.

For **Day 1**/Beginning Cycle counts:

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose (lomustine, procarbazine)
greater than or equal to 1.5	and	greater than or equal to 100	give 100%
1.0 to less than 1.5	and/or	70 to less than 100	give 80%*
less than 1.0	and/or	less than 70	Delay until ANC greater than or equal to 1.5 **AND** platelets greater than or equal to 100. Resume both drugs at 60%*

*For lomustine and procarbazine, this dose becomes the new 100% dose for subsequent treatments
If more than 2 delays, CONSULT contact physician.

For **Day 22** counts

- modify Day 1 dosing for the rest of the treatment.
- If Day 22 counts and Day 1 counts are low, the reduction is based on the lowest of the two counts (i.e., if Day 22 counts dictated a 60% dose reduction and the Day 1 counts dictated an 80% dose reduction, then the dose should be lowered to 60%)
- If dose modification is required for the first treatment cycle, reconsider the program's advisability as severe myelosuppression is common in future cycles.
- In patients with low grade gliomas, for undue toxicity switch to CNTEMOZ for remaining cycles

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose (lomustine, procarbazine)
greater than or equal to 1.5	and	greater than or equal to 100	give 100%
1.0 to less than 1.5*	and/or	75 to less than 100*	give 80%
less than 1.0*	and/or	less than 75*	give 60%

*NOTE: Patients with these variables should have careful monitoring (at least twice a week) of WBC and platelet counts. Trimethoprim/sulfamethoxazole DS one tablet po q Monday, Wednesday and Friday is recommended for patients requiring dexamethasone for longer than 4 weeks. Platelet TRANSFUSIONS for platelet less than 40 $x10^9$/L and downward trend. Consult contact physician if any questions.

2. **Renal dysfunction**: If creatinine clearance less than 50 mL/min, reconsider treatment program
3. **Hepatic dysfunction**: hold lomustine if ALT greater than 5 x ULN or bilirubin greater than 25 micromol/L until ALT less than or equal to 1.5 x ULN or bilirubin less than 25 micromol/L, then reinstitute at 60% dose.
4. **Respiratory**: Review case if complaint of shortness of breath, refer for pulmonary function testing and consider respirology referral.
5. **Intolerable side effects**: Re-evaluate treatment. For patients with low grade gliomas, switch to CNTEMOZ for remaining cycles.

PRECAUTIONS:

1. **Peripheral neuropathy**: Numbness and tingling of fingers and toes; distal weakness, foot drop; constipation; jaw pain; mild to moderate nausea/vomiting.
2. **Psycho-neurological complaints:** including drowsiness
3. **Pancytopenia:** often prolonged thrombocytopenia; possible renal damage
4. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively
5. **Extravasation**: vinCRIStine causes pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines
6. **Hypersensitivity**: Reactions are common with procarbazine. Refer to BC Cancer Hypersensitivity Guidelines. **Hypertensive crisis* if taking MAO-like drugs or foods

high in tyramine - ***diet sheet*** to be given while on procarbazine. Infrequent allergy to procarbazine includes cough.

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

References

1. Buckner JC, et al. Phase III study of radiation therapy with or without adjuvant procarbazine, CCNU, and vincristine in low-grade glioma: RTOG 9802 with Alliance, ECOG, and SWOG. J Clin Oncol 2014;32:5s (abstr 2000).