Regimen Monograph

A - Regimen Name

PCV Regimen

Procarbazine-CCNU (Lomustine)-VinCRIStine

Disease Site
Central Nervous System
(Malignant Glioma, Recurrent Malignant Glioma)

Intent
Adjuvant
Palliative

Regimen Category
Evidence-Informed :

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

Supplementary Public Funding
procarbazine
ODB - General Benefit (procarbazine)

lomustine
ODB - General Benefit (lomustine)

back to top

B - Drug Regimen

procarbazine	60 mg /m²	PO	Days 8 to 21
(*Outpatient prescription in multiples of 50mg capsules)			
lomustine	100-110 mg /m²	PO	Day 1
(*Outpatient prescription in multiples of 10, 40 & 100mg capsules)			
vinCRIStine	1.4 mg /m²	IV (maximum 2 mg)	Day 8 and 29

back to top

C - Cycle Frequency

REPEAT EVERY 42 DAYS

Adjuvant: For a usual total of 4 to 6 cycles unless disease progression or unacceptable toxicity occurs

Palliative: Until disease progression or unacceptable toxicity

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal (D29)
Consider prophylaxis daily for procarbazine
Consider prophylaxis daily for lomustine

Febrile Neutropenia Risk: Low

Other Supportive Care:

If vomiting not controlled during procarbazine treatment, escalate antiemetic treatment – vomiting may increase intracranial pressure with larger brain tumours

Also refer to CCO Antiemetic Recommendations.

back to top

E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Dosage with toxicity

Hematologic Toxicities:

Toxicity Type / Counts x 10^9 /L previous cycle	Procarbazine* (% previous dose)	Lomustine* (% previous dose)	Vincristine* (% previous dose)
Febrile Neutropenia Thrombocytopenic bleeding, grade 4 neutropenia or ≥ grade 3 thrombocytopenia	75%	75%	No change
Grade 2 neuropathy	75 %	No change	67%
Grade 3 neuropathy	Discontinue		
Other Grade 3 related organ	75%		
Grade 4 related organ or neurotoxicity	Discontinue		
Hypersensitivity, pneumonitis, renal failure, bronchospasm	Discontinue		

* Do not start new cycle until organ toxicity ≤ grade 2, platelets ≥ 100 x 10^9/L and ANC ≥ 1.5 x 10^9/L.

Hepatic Impairment

Bilirubin		AST/ALT	Procarbazine	Lomustine	Vincristine (% previous dose)
2-4 x ULN	or	2-5 x ULN	Omit	Monitor	50%
> 4 x ULN		>5 x ULN	Omit	Monitor, consider ↓	25%

Renal Impairment

Creatinine Clearance (mL/min)	Procarbazine (% previous dose)	Lomustine (% previous dose)	Vincristine (% previous dose)
>50	100%	100%	No change
10-50	75%	75%	
<10	50% or Discontinue	50% or Discontinue	

Dosage in the Elderly

Older patients may have more neurotoxicity with vincristine. No specific dosage adjustment recommended.

back to top

F - Adverse Effects

Refer to procarbazine, lomustine, vinCRIStine drug monograph(s) for additional details of adverse effects

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Nausea and vomiting • Myelosuppression (cumulative) ± bleeding, infection • CNS depression, nightmares, insomnia, hallucinations • Rash, pigmentation, radiation recall, photosensitivity • Diarrhea and stomatitis, anorexia • Neurotoxicity (cranial, peripheral ,autonomic neuropathy, disorientation, ataxia; may be severe) • Constipation, cramps (may be severe) • Fatigue, flu-like symptoms • Reproductive risks • Vesicant	• Pneumonitis / pulmonary fibrosis (may be acute or delayed) • Nephrotoxicity • Secondary leukemia, MDS • Hypersensitivity and serum sickness like reactions • Hemolytic anemia • Thromboembolism • MI, SIADH • Perforation, pancreatitis

back to top

G - Interactions

Refer to procarbazine, lomustine, vinCRIStine drug monograph(s) for additional details

back to top

H - Drug Administration and Special Precautions

Refer to procarbazine, lomustine, vinCRIStine drug monograph(s) for additional details

back to top

I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- Clinical toxicity assessment (including neurotoxicity, skin, CNS, local and pulmonary toxicity).
- CBC before each cycle.
- Baseline and regular hepatic and renal function tests
- Pulmonary function tests with prolonged (> 6month) therapy or cumulative doses > than 1,100 mg/m2

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

back to top

J - Administrative Information

Approximate Patient Visit	Vincristine: 0.5 hour
Pharmacy Workload (average time per visit)	15.99 minutes
Nursing Workload (average time per visit)	35 minutes

back to top

K - References

Buckner JC, Shaw EG, Pugh SL, et al. Radiation plus Procarbazine, CCNU, and Vincristine in Low-Grade Glioma. N Engl J Med. 2016;374(14):1344-55.

Cairncross G, Berkey B, Shaw E, et al Phase III Trial of Chemotherapy Plus Radiotherapy Compared With Radiotherapy Alone for Pure and Mixed Anaplastic Oligodendroglioma: Intergroup Radiation Therapy Oncology Group Trial 9402. J Clin Oncol 2006; 24: 2707-14.

Cairncross G, Macdonald D, Ludwin S, et al, Chemotherapy for anaplastic oligodendroglioma. J Clin Oncol 1994; 12: 2013-21.

Levin VA, Hess KR, Choucair A, et al. Phase III Randomized Study of Postradiotherapy Chemotherapy with Combination Difluoromethylornithine-PCV versus PCV for Anaplastic Gliomas. Clinical Cancer Research 2003; 9: 981–0.

Levin VA, Silver P, Hannigan J, et al. Superiority of post-radiotherapy adjuvant chemotherapy with CCNU, procarbazine, and vincristine over BCNU for anaplastic gliomas: NCOG 6G61 final report. Int J Radiat Oncol Biol Phys, 1990; 18: 321-4.

Medical Research Council Brain Tumor Working Party. Randomized trial of procarbazine, lomustine, and vincristine in the adjuvant treatment of high-grade astrocytoma: a Medical Research Council trial. J Clin Oncol 2001;19:509-18.

Murphy C, Pickles T, Knowling M, et al. Concurrent modified PCV chemotherapy and radiotherapy in newly diagnosed grade IV astrocytoma. Journal of Neuro-Oncology 2002; 57: 215–20.

van den Bent MJ, Carpentier AF, Brandes AA, et al. Adjuvant Procarbazine, Lomustine, and Vincristine Improves Progression-Free Survival but Not Overall Survival in Newly Diagnosed Anaplastic Oligodendrogliomas and Oligoastrocytomas: A Randomized European Organisation for Research and Treatment of Cancer Phase III Trial. J Clin Oncol 2006; 24: 2715-22.

PEBC Advice Documents or Guidelines

- Endorsement of the 2017 European Association for Neuro-Oncology Guideline on the Diagnosis and Treatment of Adult Astrocytic and Oligodendroglial Gliomas

July 2019 Updated hyperlink to vincristine drug monograph

back to top

M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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back to top