

PCV - Procarbazine, Lomustine and Vincristine

Indication

Palliative therapy for advanced/recurrent glioma.
Adjuvant treatment for patients with co-deleted anaplastic tumours.

ICD-10 codes

Codes prefixed with C71.

Regimen details

Day	Drug	Fluid	Route	Duration
1	Vincristine 2mg	50ml 0.9% NaCl	IV	5 mins
1	Lomustine 120mg	–	Oral	–
1 to 10	Procarbazine 150mg (50mg tds)	–	Oral	–

Cycle frequency

Every 6 weeks (42 days)

Number of cycles

6 cycles or until disease progression

Administration

Vincristine is administered as an intravenous infusion in 50mL sodium chloride 0.9% over 5 minutes. The nurse should remain with patient throughout infusion.

Lomustine is available as 40mg capsules. Lomustine capsules should be swallowed whole with water.

Procarbazine is available as 50mg capsules. Procarbazine should be swallowed whole with water.

Pre-medication

5HT₃-antagonist before lomustine on day 1 and BD on day 2.

Emetogenicity

This regimen has moderate emetogenic potential (with high emetogenic potential on days 1 and 2 due to lomustine).

Additional supportive medication

Metoclopramide 10mg po tds prn

Extravasation

Vincristine is a vesicant

Investigations – pre first cycle

Investigation	Validity period (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFT – including AST	14 days

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST)

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	Limit
Neutrophil count	$\geq 1.0 \times 10^9/\text{L}$
Platelet count	$\geq 100 \times 10^9/\text{L}$
Creatinine clearance	$\geq 60 \text{ mL/min}$
Bilirubin	$\leq 1.5 \times \text{ULN}$
AST	$< 1.5 \times \text{ULN}$

Dose modifications

• Haematological toxicity

If neutrophils $< 1.0 \times 10^9/\text{L}$ **or** platelets $< 100 \times 10^9/\text{L}$ delay one week or until recovery and consider 75% dose of lomustine and procarbazine.

If platelets $< 50 \times 10^9/\text{L}$ delay one week or until recovery and consider reducing lomustine and procarbazine to 60% dose.

In the case of febrile neutropenia (neutrophils $< 0.5 \times 10^9/\text{L}$ and fever $> 38.5^\circ\text{C}$ requiring IV antibiotics) delay one week or until FBC recovers and consider reducing lomustine and procarbazine to 75% dose.

• Renal impairment

CrCl (mL/min)	Lomustine dose	Procarbazine dose	Vincristine dose
>60	100%	100%	100%
45-60	75%	100%	100%
30-44	50%	Consider 50% dose reduction	100%
<30	Discontinue	Discontinue	Discontinue

• Hepatic impairment

Bilirubin (x ULN)	AST / ALT (x ULN)	Lomustine dose	Procarbazine dose	Vincristine dose
≤ 1.5	≤ 1.5	100%	100%	100%
1.5 - 3	1.5-3	100%	100%	50%
$>3 - 5$	$>3-5$	Consider dose reduction	Consider dose reduction	Omit
>5	>5	Consider dose reduction	Contra-indicated	Omit

• Other toxicities

Toxicity	Definition	Dose adjustment
Rash	Hypersensitivity reaction of any grade	Stop procarbazine
Neuropathy	Grade 2 (moderate symptoms)	Reduce procarbazine to 75% dose Reduce vincristine to 67% dose
	Grade 3+ (severe symptoms, limiting self-care)	Discontinue treatment

Adverse effects - for full details consult product literature/ reference texts

• Serious side effects

Myelosuppression
Pneumonitis / pulmonary fibrosis
Thromboembolism
Nephrotoxicity
Hypersensitivity and allergic reactions
Secondary malignancy
Bowel perforation
Pancreatitis
Myocardial infarction
SIADH
Teratogenicity
Infertility

• Frequently occurring side effects

Nausea or vomiting
Fatigue, flu-like symptoms
Anorexia, weight loss
Constipation, diarrhoea
Neurotoxicity
Myelosuppression
Stomatitis/mucositis

• Other side effects

Rash, pigmentation, photosensitivity
CNS depression, nightmares, hallucinations, insomnia

Significant drug interactions – for full details consult product literature/ reference texts

Coumarin-derived anticoagulants such as warfarin: patients established on warfarin should either be changed to low molecular weight heparin or have weekly monitoring of INR. Patients who are initiated on anti-coagulation should remain on low molecular weight heparin until completion of the course of chemotherapy.

Phenytoin and fosphenytoin: close monitoring and/or alternative agents are recommended if co-prescribed with this regimen. Phenytoin serum levels may be decreased, possibly as a result of decreased absorption and/or increased metabolism.

Alcohol: Procarbazine has a weak disulfiram-like effect and can lead to alcohol intolerance.

MAO inhibition: Procarbazine is a weak inhibitor of MAO and can cause CNS side-effects. Care should be taken when co-prescribing antihypertensives, CNS depressants or tricyclic antidepressants.

Barbiturates: Phenobarbital can lead to a reduced anti-tumour effect of lomustine due to induction of hepatic enzymes and increased elimination. Barbiturates can cause increased CNS depression with procarbazine.

Additional comments

Haematological toxicity may be cumulative.

Lomustine can cause pulmonary problems after high, lifetime cumulative doses ($>1,100\text{mg/m}^2$). Onset of symptoms may occur months/years after treatment discontinued.

References

- <http://www.swscn.org.uk/guidance-protocols/cancer-protocols/> accessed 10 May 2020
- Summary of Product Characteristics Lomustine (medac). www.medicines.org.uk
- Summary of Product Characteristics Procarbazine (medac). www.medicines.org.uk
- Summary of Product Characteristics Vincristine (Hospira). www.medicines.org.uk
- 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 Jan 15;19(2):509-18.

THIS PROTOCOL HAS BEEN DIRECTED BY DR BEAUMONT, DESIGNATED LEAD CLINICIAN FOR NEURO-ONCOLOGY

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

Date: June 2020

Review: June 2022

VERSION: 15
