PCV

Palliative chemotherapy for recurrent gliomas
Adjuvant therapy for Grade 2 gliomas
Neo-adjuvant or adjuvant therapy for 1p/19q co-deleted anaplastic (Grade 3) oligodendroglioma

Drugs/Dosage:	Lomustine	100mg/m^2	PO	Day 1 only
	Procarbazine	100mg/m^2	PO	once daily for 10 days, starting Day 2
	Vincristine	1.5mg/m^2 (max 2mg)	IV	Day 1 only

Administration: Vincristine diluted in 50ml 0.9% sodium chloride and infused over 5–10 minutes
Lomustine, available as 40mg capsules, to be swallowed whole with water.
Procarbazine, available as 50mg capsules, to be swallowed whole with water.

Frequency: 6 weekly cycle

Palliative use:	6 cycles, or until tumour progression
Adjuvant use:	up to 8 cycles[1], if tolerated
Neo-adjuvant use:	4 cycles before RT

Main Toxicities: myelosuppression; peripheral neuropathy; constipation; skin rashes; ovarian failure/infertility

Anti-emetics: Vincristine – mildly emetogenic
Procarbazine – moderately emetogenic
Lomustine – highly emetogenic
NB. For those patients on long-term oral dexamethasone for their brain tumour, they will not need anti-emetic doses (IV or oral) of dexamethasone.

Extravasation: Vincristine is a vesicant

Regular Investigations:	FBC	Day 1
	LFTs & U&Es	Day 1

Comments: Procarbazine is a mild MAOI – alcohol should be avoided whilst taking it.
Dietary restrictions are not required, although patients should be advised of the foods that have the rare potential to cause an unpleasant reaction (as listed in the procarbazine PIL provided by Pharmacy).

Dose Modifications

Haematological Toxicity: Note: Lomustine may cause permanent haematological damage with prolonged use.

WBC < 3.0 x 10^9/l	Delay treatment for 2 weeks.
or	Repeat FBC and, if within normal parameters,
Platelets < 100 x 10^9/l	proceed at full dose.

If FBC still low after a 2 week delay, repeat blood counts at further 2 weekly intervals until satisfactory and then treat with 50% dose of lomustine and full dose of procarbazine and vincristine.

If FBC still low at 12 weeks (i.e. after a 6 week delay), discontinue lomustine.

Renal Impairment:

CrCl (ml/min)	Lomustine Dose
> 60	Give 100%
45 – 60	Give 75%
30 - 45	Give 50%
< 30	Not recommended

For **procarbazine**, if serum creatinine > 177µmol/l, give 50% dose, and not recommended with severe renal failure.

Hepatic Impairment:

Bilirubin (µmol/l)		ALT / AST (units/l)	Vincristine Dose
26 – 51	**or**	60 – 180	Give 50%
> 51	**and**	Normal	Give 50%
> 51	**and**	> 180	Omit

Bilirubin (µmol/l)		AST (units/l)	Procarbazine Dose
> 50		-	Consider 50% dose reduction
> 85	**or**	> 180	Contra-indicated

Neuropathy: Vincristine should be reduced to 1mg/m^2 in the presence of Grade 2 neuropathy (severe paraesthesia and mild weakness).
Vincristine should be discontinued in the presence of Grade 3 -4 neuropathy.

Reference:
Shaw, E et al; JCO 2012; 30: 3065 – 3070
Van Den Bent; JCO 2013; 31 (3): 344
Cairncross, G et al; JCO 2013; 31 (3): 337
[1]RTOG 9802 and EORTC 26951 delivered PCV as 6 cycles but with an 8 week cycle length (and not with identical drug doses) – but the decision has been made to avoid having more than one Alliance version of PCV