Lomustine, Cisplatin and Vincristine (CCisV)

Indication
Adjuvant treatment for adult patients with medulloblastoma.

Regimen details

Day	Drug	Route	Fluid	Time
1	Lomustine 75mg/m^2	Oral		Stat
	Vincristine 1.5mg/m^2 (max 2mg)	IV	50ml 0.9% sodium chloride	5 mins
	20mmol potassium chloride & 10mmol magnesium sulphate	IV	1 litre 0.9% sodium chloride	2 hours
	Cisplatin 70mg/m^2	IV	1 litre 0.9% sodium chloride	2 hours
	20mmol potassium chloride & 10mmol magnesium sulphate	IV	1 litre 0.9% sodium chloride	2 hours
8	Vincristine 1.5mg/m^2 (max 2mg)	IV	50ml 0.9% sodium chloride	5 mins
15	Vincristine 1.5mg/m^2 (max 2mg)	IV	50ml 0.9% sodium chloride	5 mins

Cycle frequency
Every 6 weeks (42 days)

Number of cycles
6 cycles

Administration
As per regimen details

Pre-medication
Dexamethasone, aprepitant, ondansetron and olanzapine

Emetogenicity
This regimen has high emetogenic potential

Additional supportive medication
Metoclopramide 10mg po tds prn

Extravasation
Vincristine and Cisplatin are vesicants.

Investigations – pre first cycle

Investigation	Validity period
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	≥ 1.0 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Creatinine clearance	≥ 60 mL/min
Bilirubin	≤ 1.5 x ULN
AST	< 1.5 x ULN

Dose modifications

- **Haematological toxicity**

Neutrophils < 1 or platelets <100	Delay chemotherapy for at least 1 week
If lack of recovery after > 2 weeks (neutrophils <1 or platelets <100)	Give cisplatin and vincristine (omit lomustine)
If recovered prior to next cycle	Reintroduce lomustine at 50mg/m^2
If neutrophils < 0.5 and episode of neutropenic fever at any time	Reduce lomustine to 50mg/m^2
If further episode of neutropenia and fever	Reduce cisplatin to 50mg/m^2
If platelets < 30 and/or platelet transfusion required	Reduce lomustine to 50mg/m^2
If further episode of thrombocytopenia (platelets <30)	Omit lomustine

- **Renal impairment**

GFR(ml/min)	**Cisplatin dose**	**Lomustine dose**
>60	100%	100%
45-59	75%	75%
30-45	Consider carboplatin (AUC5)	50%
<30		Not recommended

- **Hepatic impairment**

Bilirubin/μmol/L	**AST/ALT /units**	**Vincristine Dose**
26-51	or 60-180	50%
>51	and below upper limit of normal	50%
>51	and >180	Omit

- **Other toxicities**

Ototoxicity

Brock / CTC (SIOP) Grading:

0 Loss < 40 db on all frequencies
1 Loss at least 40 db at 8000 Hz
2 Loss at least 40db at 4000 Hz
3 Loss at least 40 db at 2000 Hz
4 Loss at least 40 db at 1000 Hz

Grade	**Modification**
0-1	None
2	Substitute carboplatin AUC5 for cisplatin
3-4	Omit platinum

Neurotoxicity

Vincristine associated seizures or ileus. N.B. Rule out SIADH as a cause of seizures.	Omit vincristine during current cycle of chemotherapy and reduce by 25% for next cycle. If seizures or ileus do not recur, then return to full dose.
Parasthesia, weakness, abdominal pain or constipation	Omit next vincristine dose but on recovery reintroduce at 25% dose increasing to full dose if symptoms do not return

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
Ototoxicity

- **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.
Barbiturates: Phenobarbital can lead to a reduced anti-tumour effect of lomustine due to induction of hepatic enzymes and increased elimination.

Additional comments

Haematological toxicity may be cumulative.
Lomustine can cause pulmonary problems after high, lifetime cumulative doses (>1,100mg/m^2). Onset of symptoms may occur months/years after treatment discontinued.

References

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

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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