JAKACKI protocol – part 1 Carboplatin & Vincristine

Indication
Concomitant chemo-radiotherapy for high risk medulloblastoma

ICD-10 codes
Codes prefixed with C71.

Regimen details
Group 3 tumours only

Day	Drug	Dose	Route
1	Vincristine	1.5mg/m^2 (max. 2mg)	IV infusion
1-5	Carboplatin	35mg/m^2	IV infusion

OR

Other subgroups

Day	Drug	Dose	Route
1	Vincristine	1.5mg/m^2 (max. 2mg)	IV infusion

Treatment should start within 40 days of surgical resection, earlier if biopsy only. Carboplatin should start on day one of craniospinal radiotherapy and is then given on each radiotherapy treatment day, 1-4 hours prior to radiotherapy for 30 of the 31 radiotherapy fractions. If vincristine alone, treatment can start on any day within the first week of radiotherapy and is then administered on the same day each week.

Cycle frequency
7 days

Number of cycles
6 cycles

Administration
Vincristine is administered as an intravenous infusion in 50mL sodium chloride 0.9% over 10 minutes, as per national guidance. The nurse should remain with patient throughout infusion.

Carboplatin is administered over 15 minutes 1-4 hours prior to daily radiotherapy for the first 30 of the 31 radiotherapy fractions.

Patients should be observed closely for hypersensitivity reactions, particularly during the first and second infusions. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of carboplatin. Facilities for the treatment of hypotension and bronchospasm must be available.

If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require discontinuation of therapy. The infusion may be temporarily interrupted and when symptoms improve restarted at a slower infusion rate. Chlorphenamine 10mg IV may be administered. Severe reactions, such as hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of carboplatin and appropriate therapy.

Pre-medication

Nil

Emetogenicity

Carboplatin and Vincristine - this regimen has moderate emetogenic potential. Single agent 5HT-3 antagonists should be prescribed, and corticosteroids should be avoided if possible during chemotherapy administration in view of their effect on the blood-brain barrier but can be used if severe nausea and vomiting occurs.

Vincristine alone - this regimen has mild emetogenic potential

Additional supportive medication

GCSF if required (see haematological toxicity)
Laxatives as per local guidance
Mouthwashes as per local policy.

Extravasation

Vincristine is a vesicant (Group 5).
Carboplatin is an irritant (Group 3)

Investigations – pre first cycle

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

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	72 hours*
U+E (including creatinine)	72 hours
LFT	72 hours

* FBC should be checked on Monday, Wednesday & Friday during treatment. U&Es & LFTs are checked once weekly depending on the day that treatment is started.

On completion of the six weeks of chemotherapy, FBC should be checked twice per week until platelets ≥100 x 10^9/L and neutrophil ≥ 1.5 x 10^9/L. Once this is achieved phase 2 can commence (see separate protocol). Platelets should still be maintained ≥ 30 x 10^9/L during this period.

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant for the non-haematological toxicity, **except for cycle 1, day 1when authorisation from prescriber/consultant must be given for all blood results.**

Investigation	**Limit**
Neutrophil Count	≥ 1.5 x 10^9/L (see below)
Platelet Count	≥ 30 x 10^9/L (see below)
Haemoglobin	≥ 100g/L (see below)
Creatinine clearance	≥ 50mL/min
Bilirubin	< 51µmol/L
ALT	< 5 x ULN

Dose modifications

- **Haematological toxicity**

Treatment should **not** be delayed for myelosuppression unless patient is clinically unwell. Recommendations below regarding management of cytopenias should be followed. **If the patient is unwell, including with sepsis, decision to proceed with treatment should be discussed with a consultant**.

Haemoglobin should be maintained ≥ 100g/L. If Hb <100g/L arrange blood transfusion.

Platelets should be maintained ≥ 30 x 10^9/L. If <30 x 10^9/L arrange platelet transfusion, consider repeat FBC to ensure increment, and arrange repeat FBC at 48 hours for monitoring.

Any changes to the minimum Hb and platelet levels required for treatment to proceed will be documented by the prescriber.

If neutrophils <1.5 x 10^9/L, please follow the table below:

Guideline for GCSF Administration during Radiotherapy		
Day	ANC 1.0-1.5 x 10^9/L	ANC <1.0 x 10^9/L
Friday	0.5million units/kg/day Fri/Sat/Sun	0.5million units/kg/day Fri/Sat/Sun
Monday	No G-CSF	0.5million units/kg/day Mon/Tues
Wednesday	No G-CSF	0.5million units/kg/day Wed/Thurs

- **Renal impairment**

Carboplatin - patients with impaired kidney function are likely to experience more severe and prolonged myelotoxicity. Discuss with consultant and consider dose reduction if calculated creatinine clearance <50mL/min. If <20mL/min consider omitting or changing treatment choice.

Vincristine – no dose adjustments required

- **Hepatic impairment**

Bilirubin (µmol/l)	**Vincristine dose**
<51	100%
51-180	50%
>180	Omit

Transient increases in liver enzymes may be seen in patients being treated with carboplatin although no dose reduction is usually required. If bilirubin ≥ 3 x ULN and/or ALT ≥ 5 x ULN discuss with consultant.

- **Other toxicities**

Vincristine dose should be omitted and then reduced to 1mg/m^2 (max dose 1.5mg) for future doses on recovery after discusssion with consultant in the following circumstances:

- Grade 3 – 4 foot drop
- Severe Paresis
- Disabling paraesthesia
- Ileus

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

- **Serious side effects**

Myelosuppression
Infertility
Hypersensitivity reactions
Nephrotoxicity
Neuropathy and neuritic pain
Haemolytic-uraemic syndrome
Reversible Posterior Leukoencephalopathy Syndrome (RPLS)
Syndrome of inappropriate secretion of antidiuretic hormone (SIADH)

- **Frequently occurring side effects**

Hypersensitivity reactions
Myelosuppression
Nausea and vomiting
Constipation
Stomatitis and mucositis
Fatigue
Rash
Oedema
Ototoxicity
Electrolyte disturbances
Pain

- **Other side effects**

Taste disturbances

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

Warfarin/coumarin anticoagulants: Avoid use due to elevations in INR. Switch to low molecular weight heparin during treatment.
Carboplatin:
Aminoglycoside antibiotics: increased risk of nephrotoxicity and ototoxicity
Clozapine: increased risk of agranulocytosis, avoid concomitant use
Diuretics: increased risk of nephrotoxicity and ototoxicity
Nephrotoxic drugs: increased nephrotoxicity; not recommended
Phenytoin: carboplatin reduces absorption and efficacy of phenytoin
Vincristine:
Azoles antifungals: Azoles such as Fluconazole can increase the exposure of Vincristine. Avoid the use of Azoles 48 hours either side of Vincristine dose. There is also an increased risk of hepatoxicity with concomitant use.
Phenytoin – Phenytoin can decrease the exposure to Vincristine and can increase the risk of peripheral neuropathy.

References

- Childrens Oncology Group – Efficacy of Carboplatin Administered Concomitantly with Radiation and Isotretinoin as a Pro-Apoptotic Agent in Other Than Average Risk Medulloblastoma/PNET Patients
- Jakacki R, Burger P et al Outcome of children with Metastatic Medulloblastoma Treated With Carboplatin During Craniospinal Radiotherapy: A Children's Oncology Group Phase I/II study JCO vol 30 No.21 (2012) p2648 – 2653
- Krens, S et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20: e200–07
- Leary, S et al. Efficacy of Carboplatin and Isotretinoin in Children with High-Risk Medulloblastoma: A Randomized Clinical Trial From the Children's Oncology Group. Jama Oncol 2021; Sep 1;7(9):1313-1321
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- Summary of Product Characteristics Carboplatin Solution for Infusion (Hospira) Accessed 16 October 2025 via www.medicines.org.uk

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