CAV – Cyclophosphamide, Doxorubicin and Vincristine (lung)

Indication
Second or third line chemotherapy for small cell lung cancer.

ICD-10 codes
Codes with a prefix C34

Regimen details

Day	Drug	Dose	Route
1	Vincristine	1.4mg/m^2 (max 2mg)	IV infusion
1	Cyclophosphamide	750mg/m^2	IV infusion
1	Doxorubicin	50mg/m^2	IV bolus

Cycle frequency
21 days

Number of cycles
4 - 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.

Doxorubicin is administered by slow IV bolus into the arm of a fast running drip of sodium chloride 0.9%.

Cyclophosphamide is given as an IV infusion in 250-500mL sodium chloride 0.9% over 30 minutes.

Pre-medication
Antiemetics as per local policy.

Emetogenicity
This regimen has moderate emetic potential

Additional supportive medication
Ciprofloxacin 250mg BD and fluconazole 50mg OD should be considered for patients with extensive disease or poor performance status.

Extravasation
Vincristine and doxorubicin are vesicant (Group 5)
Cyclophosphamide is neutral (Group 1)

Investigations - pre first cycle

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

ECHO or MUGA if significant cardiac history or previous anthracycline treatment.

Investigations - pre subsequent cycles

Investigation	**Validity period** (or as per local practice)
FBC	96 hours
U+E (including creatinine)	7 days
LFTs	7 days

Standard limits for administration to go ahead

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

Investigation	**Limit**
Neutrophils	≥ 1.5 x 10^9/L
Platelets	≥ 100 x 10^9/L
Creatinine Clearance (CrCl)	> 20 mL/min
Bilirubin	≤ 1.5 ULN
AST/ALT	≤ 1.5 x ULN

Dose modifications

- **Haematological toxicity**

If neutrophils <1.5 x 10^9/L and/or platelets <100 x 10^9/L delay 1 week or until recovery.

If febrile neutropenia or neutrophils < 0.5 x 10^9/L for more than 1 week reduce doses of doxorubicin and cyclophosphamide to 75% for future cycles. Consider prophylactic ciprofloxacin and fluconazole (see additional supportive medication).

- **Renal impairment**

CrCl (mL/min)	**Cyclophosphamide dose**
> 20	100%
10-20	75%
<10	50%

There is no data available on the use of doxorubicin in severe renal impairment. Consider dose reduction if CrCl <10mL/min (consultant decision).
No dose modifications required for vincristine in renal impairment.

- **Hepatic impairment**

Bilirubin (x ULN)		**AST/ALT** (x ULN)	**Vincristine dose**
< 1.5	and	< 1.5	100%
1.5 – 3.0	or	1.5- 3.5	50%
> 3.0	and	≤ 1.5	50%
> 3.0	and	> 3.5	Omit

Bilirubin (x ULN)	**Doxorubicin dose**
< 1.5	100%
1.5-3.0	50%
3.0-5.0	25%
>5.0	Omit

If AST/ALT 2-3 x ULN reduce doxorubicin dose to 75%. If AST/ALT > 3 x ULN reduce doxorubicin dose to 50%.

Cyclophosphamide is not recommended if bilirubin > 1.5 x ULN or AST/ALT > 3 x ULN (consultant decision).

- **Other toxicities**

If grade 2 neuropathy reduce vincristine dose to 50%, if grade ≥ 3 neuropathy discontinue.

Any other grade 3 or 4 toxicity- discuss with consultant.

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

- **Serious side effects**

Myelosuppression
Teratogenicity
Infertility
Cardiotoxicity
Peripheral neuropathy

- **Frequently occurring side effects**

Diarrhoea
Constipation
Fatigue
Nausea and vomiting
Myelosuppression
Stomatitis and mucositis
Arthralgia and myalgia
Alopecia

- **Other side effects**

Phlebitis
Taste disturbances
Bladder irritation

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

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

Cyclophosphamide:
Amiodarone: increased risk of pulmonary fibrosis – avoid if possible
Clozapine: increased risk of agranulocytosis – avoid concomitant use
Digoxin tablets: reduced absorption – give as liquid form
Indapamide: prolonged leucopenia is possible - avoid
Itraconazole: may increase adverse effects of cyclophosphamide
Phenytoin: reduced absorption - may need to increase dose of phenytoin
Grapefruit juice: decreased or delayed activation of cyclophosphamide. Patients should be advised to avoid grapefruit juice for 48 hours before and on day of cyclophosphamide dose.

Additional comments

Patients should be advised to avoid grapefruit juice for 48 hours before and on day of cyclophosphamide dose.

Cardiotoxicity has been associated with anthracyclines, with adverse events being more common in patients with a prior history of coronary artery disease. Caution must be taken in patients with a history of significant cardiac disease, arrhythmias or angina pectoris.

Doxorubicin has a life time maximum cumulative dose of 450mg/m^2

References

- Summary of Product Characteristics Vincristine (Hospira). Accessed 25 Sept 2014 via www.medicines.org.uk
- Summary of Product Characteristics Cyclophosphamide accessed 25 Sept 2014 via http://www.mhra.gov.uk/Safetyinformation/Medicinesinformation/SPCandPILs
- Summary of Product Characteristics Doxorubicin (Hospira) accessed 25 Sept 2014 via www.medicines.org.uk
- Roth, BJ et al, JCO, 1992; Vol 10 (2): 282-291

Written/reviewed by: Dr A Dangoor (Consultant Oncologist, UHBristol NHS Trust), Dr P Jankowska (Consultant Oncologist, Taunton and Somerset NHS Trust)

Checked by: Sarah Murdoch (Senior Oncology Pharmacist, SW Strategic Clinical Network)

Authorised by: Dr J Braybrooke (Consultant Oncologist, UHBristol NHS Trust, SW Strategic Clinical Network)

Date: 13 November 2014
