CAV (Cyclophosphamide, Doxorubicin, Vincristine)

Indication

Relapsed small cell lung cancer
Relapsed small cell carcinoma of any primary site

Regimen details

Vincristine 1.3mg/m^2 (max 2mg) intravenous over 5 minutes in 50ml 0.9% sodium chloride
Doxorubicin 40mg/m^2 intravenous bolus
Cyclophosphamide 750mg/m^2 intravenous bolus

Cycle frequency

Given every 3 weeks

Number of cycles

4-6 cycles

Administration

Vincristine is for intravenous administration only. Administration by other routes may be fatal
Prior to starting vincristine, ensure the venous access device is sufficiently patent by flushing well with sodium chloride 0.9%. If there is doubt about the patency of the access device, it must not be used
Vincristine is to be given by intravenous infusion over 5 minutes
Vincristine is highly vesicant – during administration a nurse should remain with the patient and observe the infusion site carefully for signs of extravastation. In the event that extravasation is suspected, the infusion must immediately be stopped and appropriate treatment started (see extravasation policy)

Doxorubicin and cyclophosphamide are given by intravenous injection into a fast flowing drip

Pre-medication

None

Emetogenicity

High

Additional supportive medication

Consider GCSF if previous neutropenic sepsis

Extravasation

Vincristine and doxorubicin are vesicant
Cyclophosphamide is neutral

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	≥ 1.5 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Creatinine clearance	See below
Bilirubin	See below
AST	See below

Dose modifications

Haematological toxicity:

Reduce cyclophosphamide and doxorubicin by 25% in the event of prolonged (>1 week) delay due to neutropenia or thrombocytopenia

Renal Function If Cr > 300 µmol/l withhold cyclophosphamide:

CrCl (or GFR)	Cyclophosphamide Dose
> 20 ml/min	100%
10-20 ml/min	75%
< 10 ml/min	50%

Hepatic function

Bilirubin		AST/ALT	Doxorubicin Dose
< ULN	And	< 2x ULN	100%
<ULN	And	2-3x ULN	75%
ULN – 2.5x ULN	Or	> 3x ULN	50%
2.5 – 4x ULN			25%
> 4x ULN			Omit

Bilirubin		ALT	Vincristine Dose
< ULN		-	100%
ULN – 2.5x ULN	Or	2 – 3x ULN	50%
> 2.5x ULN	And	Normal	50%
> 2.5x ULN	And	ALT > 6x ULN	Omit

Reduce cyclophosphamide dose by 25% if bilirubin 2.5 – 4x ULN
Cyclophosphamide is not recommended if 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

Nausea & Vomiting
Constipation
Alopecia
Interstitial pneumonitis, pulmonary fibrosis
Discoloured urine
Haemorrhagic cystitis
Cardiomyopathy and arrhythmias
Peripheral neuropathy
Autonomic neuropathy
Hyperpigmentation
Hepatocellular necrosis

Bone Marrow Depression; anaemia, neutropenia, thrombocytopenia

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

Northern Cancer Alliance protocol - https://www.northerncanceralliance.nhs.uk/wp-content/uploads/2018/11/VAC-CAV-protocol-CRP09-L003-V1.5.pdf

SWAG Cancer Alliance protocol - https://www.swagcanceralliance.nhs.uk/wp-content/uploads/2020/09/TopotecanNEW21.pdf

THIS PROTOCOL HAS BEEN DIRECTED BY DR LAU, DESIGNATED LEAD CLINICIAN FOR LUNG CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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