Systemic Anti-Cancer Treatment Protocol

Cyclophosphamide, Doxorubicin & Vincristine (CAV)

PROTOCOL REF: MPHACAVLU
(Version No: 1.0)

Approved for use in:

Second line chemotherapy in small cell lung cancer

Small cell cancer of any site, e.g. bladder

Dosage:

Drug	Dose	Route	Frequency
Cyclophosphamide	**750mg/m^2**	IV	Every 21 days
Doxorubicin	**50mg/m^2**	IV	Every 21 days
Vincristine	**1.4mg/m^2 (max 2mg)**	IV	Every 21 days

Cycle is repeated every 21 days for 6 cycles followed by review

Supportive Treatments

Anti-emetic risk - Moderate

Dexamethasone 4mg twice daily for 3 days

Domperidone 10mg tablets, to be taken up to three times a day when required

Extravasation risk:

Doxorubicin is a vesicant. Erythematous streaking along the vein proximal to the site of injection has been reported, and must be differentiated from an extravasation event. This reaction usually subsides within 30 minutes.

Cyclophosphamide – Non vesicant

Vincristine – vesicant

Refer to the network guidance for the prevention and management of extravasation

Administration:

Day	Drug	Dose	Route	Diluent and rate
1	**Dexamethasone**	**12mg**	PO	30mins before chemotherapy
	Ondansetron	**24mg**	PO	30mins before chemotherapy
	Doxorubicin	**50mg/m^2**	IV	Over 15 to 30 minutes alongside fast flowing sodium chloride 0.9%
	Vincristine	**1.4mg/m^2 (max 2mg)**	IV	Sodium chloride 0.9% 50mL over 15 minutes
	Cyclophosphamide	**750mg/m^2**	IV	Over 30 minutes

Notes:

- Nasal stuffiness can occur immediately with administration of cyclophosphamide, if uncomfortable for the patient the drug can be slowed down
- Encourage an oral fluids intake of 2 litres per day to promote urinary output & prevent chemical cystitis with cyclophosphamide.
- Red urine is likely following doxorubicin

Maximum cumulative doxorubicin dose is 450 to 550 mg/m^2**.**

Cardiac ejection fraction must be > 50% to proceed with the regimen

Perform baseline LVEF evaluation on patients suspected of having impaired cardiac contractility

Main Toxicities:

Myelosuppression: neutropenia, thrombocytopenia, anaemia

Alopecia, nausea and vomiting, diarrhoea, stomatitis,

Hypersensitivity: including anaphylaxis, rash and oedema

Cyclophosphamide
Haematuria may occur during or after treatment. Skin pigmentation, typically affecting the palms and nails of the hands and the soles of the feet Inappropriate secretion of anti-diuretic hormone, fluid retention and hyponatremia, myocardial toxicity especially at high dosage. Rarely pulmonary fibrosis, hepatic toxicity

Doxorubicin
Cardiotoxicity life-threatening congestive cardiomyopathy, sinus tachycardia, ventricular tachycardia, tachyarrhythmia, bradycardia.
Vincristine
Neuropathy, arthralgia, myalgia Polyuria, dysuria and urinary retention due to bladder atony have occurred. Hypertension and hypotension

Investigations:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Medical Assessment	X		X		X	At end of treatment
Nursing Assessment		X	X	X	X	Every cycle
Respiratory Rate and O_2 sats	X	X	X	X	X	Every cycle
FBC	X		X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	Every Cycle
Serum Cr	X	X	X	X	X	Every cycle
MUGA**	X					If clinically indicated
CT scan	X				X	At end of treatment
Informed Consent	X					
ECG	X					As clinically indicated
Blood pressure	X					Repeat if clinically indicated

PS recorded	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	Every cycle

*Calculate CrCl if changes of > 30% to Sr Creatinine

**Baseline MUGA if suspected cardiac contractility impairment – repeat during treatment if clinically indicated

Dose Modifications and Toxicity Management:

Haematological Toxicity:

Proceed on day 1 if-

Plt ≥ 100 x 10^9/L	ANC ≥ 1.0 x 10^9/L

Delay 1 week on day 1 if-

Plt ≤ 99 x 10^9/L	ANC ≤ 0.9 x 10^9/L

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

If > 1 week delay consider 25% dose reduction for cyclophosphamide and doxorubicin for subsequent cycles

Hepatic impairment:

	Doxorubicin	**Vincristine**	**Cyclophosphamide**
Bilirubin µmol/L	**Dose**	**Dose**	**Dose**
24 to 50	50%	50%	100%
51 to 85	25%	50% (if ALT within normal limits)	75%
Above 85	Omit	Omit	Omit

Renal impairment:

No dose adjustments are required for moderate renal impairment

References:

- Cyclophosphamide 50 Tablets. Summary of Product Characteristics, Pharmacia, Kent.16/08/2002. Available from www.medicines.org.uk/emc/medicine. Last updated 26/03/2012.

- Doxorubicin 2mg/ml Concentrate for Solution for Infusion. Summary of Product Characteristics. Pfizer Limited, Sandwich, Kent. 22/06/2009. Available from www.medicines.org.uk/emc/medicine. Last updated 09/08/2012

- Oncovin (Vincristine Sulphate Ph.Eur).Summary of Product Characteristics. Genus Pharmaceuticals, Berkshire.23/07/2008. Available from www.medicines.org.uk/emc/medicine. Last Updated 17/02/2014

- Dosage Adjustment for Cytotoxics in Hepatic Impairment January 2009 UCLH - Dosage Adjustment for Cytotoxics in Hepatic Impairment (Version 3 - updated January 2009)

- Dosage Adjustment for Cytotoxics in Renal Impairment January 2009 UCLH - Dosage Adjustment for Cytotoxics in Renal Impairment (Version 3 - updated January 2009)