Systemic Anti Cancer Treatment Protocol

EC (Epirubicin Cyclophosphamide) Advanced Breast Cancer Regimen

PROTOCOL REF: MPHAECBR
(Version No: 1.0)

Approved for use in:

Locally advanced and/or metastatic breast cancer not previously treated with anthracycline based regimen

Dosage:

Drug	Dosage	Route	Frequency
Epirubicin	**90mg/m²**	**IV**	Every 21 days For 6 cycles
Cyclophosphamide	**600mg/m²**	**IV**	

For patients where clinical concern about potential for toxicity, then dose reduction to 60mg/m^2 or 75mg/m^2 are also acceptable starting doses.

Supportive treatments

Dexamethasone 4mg orally twice a day for three days

Ondansetron 8mg orally twice a day for three days

Domperidone 10mg tablets three times a day when required

Notes:

Maximum cumulative dose of epirubicin: 900 to 1000 mg/m$^{2.}$ Ensure all adjuvant treatment is included and any treatment for other tumours e.g. previous lymphoma

Perform baseline ejection function assessment (ECHO or MUGA) if patient is considered at risk of significantly impaired cardiac contractility.

Use alternative regimen if cardiac ejection fraction < 50%

Extravasation risk:

Epirubicin: 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 – neutral

Administration:

Day	Drug	Dose	Route	Diluent and rate
1	**Ondansetron tablets** 30mins before chemotherapy	**24mg**	**PO**	
	Dexamethasone tablets 30mins before chemotherapy	**12mg**	**PO**	
	Epirubicin	**90mg/m^2**	**IV**	IV bolus over 10 to 15 minutes Concurrent administration, doxorubicin at 400mL/hr and sodium chloride 0.9% at 100mL/hr
	Cyclophosphamide	**600mg/m^2**	**IV**	IV bolus over 30 minutes

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

Main Toxicities:

Haematological	Neutropenia, thrombocytopenia and anaemia.
Gastrointestinal	Nausea, vomiting, stomatitis, diarrhoea, mucositis
Cardiotoxicity	Epirubicin - sinus tachycardia and/or electrocardiogram (ECG) abnormalities such as non-specific ST-T wave changes. Congestive heart failure. Other cardiac events have been reported, included delayed toxicity.
Dermatological	Alopecia, normally reversible, although can be permanent following docetaxel.
Urological	Red colouration of urine for 1 to 2 days after administration following epirubicin Urotoxicity can occur with short-term and long-term use of cyclophosphamide. Hemorrhagic cystitis, pyelitis, ureteritis, and haematuria. Mesna can be given if required.
Ocular	Watery eyes, gritty and irritated
Infertility	Amenorrhea, risk of premature menopause However ensure appropriate contraceptive advice is given

Investigations:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Comments
Medical Assessment	X		X		X	Alternate cycles
Nursing Assessment	X	X	X	X	X	Every cycle
ECHO / ECG	X					If clinically indicated
FBC	X	X	X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	Every cycle
Informed Consent	X					
CT scan	X					After 6 cycles
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

ECHO/ECG at baseline if pre-existing cardiac risk factors

Dose Modifications and Toxicity Management:

Haematological Toxicity:

Proceed with treatment if;

Neutrophils $\geq$ 1.0 **and** platelets $\geq$ 100 x 10^9/L

Defer by 7 days or until blood counts recovered if neutrophils $\leq$ 1.0 **or** platelets $\leq$ 100 x 10^9/L

Second episode or severe febrile neutropenia: Defer by 7 days or until blood counts recovered if neutrophils $\leq$ 1.0 **or** platelets $\leq$ 100 x 10^9/L **and reduce** to 80% dose

Hepatic impairment:

	Epirubicin	Cyclophosphamide
Bilirubin µmol/L	**Dose**	**Dose**
24 to 50	50%	100%
51 to 85	25%	75%
Above 85	Omit	Omit

Renal impairment:

No dose adjustments required for moderate renal impairment.

References:

EC versus ED

Blohmer J et al, Annals of Oncology 21(7):1430-1435

The Renal Drug Handbook 4th edition, Ashley C and Dunleavy A. Radcliffe Publishing. 2014