Systemic Anti Cancer Treatment Protocol

EC – D
Epirubicin, Cyclophosphamide followed by Docetaxel

PROTOCOL REF: MPHAECDBR
(Version No: 1.0)

Approved for use in:

Adjuvant or Neo-adjuvant Breast: ER positive, HER2 negative ("luminal A/B"). Fit, moderate to high risk patients.

NB: paclitaxel EC may be more appropriate for patients aged 60 years and over or if surgical wound healing is prolonged

Dosage:

Drug	Dosage	Route	Frequency
Epirubicin	90mg/m²	IV	Cycles 1 to 3 Day 1 only of a 21 day cycle
Cyclophosphamide	600mg/m²	IV	
Followed by			
Docetaxel	100mg/m²	IV	Cycles 4 to 6 Day 1 only of a 21 day cycle

Supportive Treatments:

Ondansetron 8mg orally twice a day for three days

Domperidone 10mg tablets, three times a day as required

Filgrastim subcutaneous injection daily for 7 days from day 3 (dose of 300 micrograms for patients below 70kg, and 480 micrograms for those 70kg and above)

Additional item EC – cycles one to three

Dexamethasone 4mg orally twice a day for three days

Additional item Docetaxel – cycles four to six

Premedication of dexamethasone 8 mg twice daily for 3 days starting 1 day prior to docetaxel administration

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

Docetaxel: exfoliant

Administration:

EC Cycles 1 to 3

Day	Drug	Dose	Route	Diluent and rate
1	**Ondansetron** 30mins before chemotherapy	**24mg**	**PO**	
	Dexamethasone 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

Repeat every 21 days for 3 cycles – at cycle 3 ensure patient has dexamethasone for prior to docetaxel

- 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.

Docetaxel Cycles 4 to 6

Day	Drug	Dose	Route	Diluent and rate
Premedication: Dexamethasone 8 mg twice daily for 3 days starting 1 day prior to docetaxel administration				
1	**Ondansetron** 30mins before chemotherapy	**8mg**	**Oral**	
1	**Docetaxel**	**100mg/m^2**	**IV**	**250mL 0.9% sodium chloride over 60 minutes**

Repeat every 21 days for 3 cycles

The infusion volume for docetaxel may increase to 500mL depending on the dose to be administered

If oral dexamethasone has not been taken then an intravenous dose of 8mg can be administered on the day of treatment, in addition to the oral dose of 8mg

Switch to paclitaxel

If severe toxicity from docetaxel then consider switch to weekly paclitaxel with 3 weeks of weekly paclitaxel for each docetaxel dose.

If surgical healing is delayed then weekly paclitaxel can be administered as the first part of the regimen

Day	Drug	Dose	Route	Diluent and rate
1	Dexamethasone	8mg (reduce to 4mg for week 2)	IV bolus	30 minutes before chemotherapy
1	Ranitidine	50mg	IV bolus	30 minutes before chemotherapy
1	Chlorphenamine	10mg	IV bolus	30 minutes before chemotherapy
1	**Paclitaxel**	**80mg/m^2**	**IV Infusion**	**250mL sodium chloride 0.9% over 60 minutes**

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.
Respiratory	Acute respiratory distress syndrome, pneumonitis
Dermatological	Alopecia, normally reversible, although can be permanent following docetaxel. Docetaxel: Brittle, chipped and ridged nails
Urological	Red colouration of urine for 1 to 2 days after administration following epribucin 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
Hypersensitivity reactions	Reactions may occur within a few minutes following the initiation of treatment with docetaxel, facilities for the treatment of hypotension and bronchospasm should be available. If hypersensitivity reactions occur, minor symptoms such as flushing or localised rash with or without pruritus do not require interruption of therapy. However, severe reactions, such as severe hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of docetaxel and appropriate treatment. Patients who have developed severe hypersensitivity reactions should not be re-challenged with

	docetaxel.
Nervous system	Docetaxel: peripheral neuropathy is very common
Musculoskeletal	Arthralgia, myalgia common with docetaxel
Infertility	Amenorrhea, risk of premature menopause However ensure appropriate contraceptive advice is given

Investigations and Treatment Plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Comments
Medical Assessment	X		X		X		X	Alternate cycles
Nursing Assessment	X	X	X	X	X	X	X	Every cycle
ECHO / ECG	X							If clinically indicated
FBC	X		X	X	X	X	X	Every cycle
U&E & LFT	X		X	X	X	X	X	Every cycle
Informed Consent	X							
PS recorded	X	X	X	X	X	X	X	Every cycle
Toxicities documented			X	X	X	X	X	Every cycle
Weight recorded	X	X	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 neutropenic sepsis: Defer by 7 days or until blood counts recovered if neutrophils ≤ 1.0 **or** platelets ≤ 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%
> 85	Omit	Omit

Docetaxel
If Bilirubin >22µmol/L +/or ALT/AST >3.5 times ULN with ALP > 6 times ULN, docetaxel should not be used unless strictly indicated. ALT +/or AST > 1.5 times ULN and ALP > 2.5 times ULN – give 75mg/m^2

Renal impairment:

No dose adjustments required for moderate renal impairment.

Peripheral Neuropathy

NCI-CTC grade 2 peripheral neuropathy: withhold docetaxel until neuropathy recovers to grade 1 then dose reduce by 20%

If NCI-CTC grade 3 (or persistent grade 2) peripheral neuropathy occurs, discontinue docetaxel and consider completing course with further EC cycles

References:

PACS01 trial
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