PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Epirubicin Weekly Advanced Breast Cancer

PROTOCOL REF: MPHAEPWEBR
(Version No. 1.1)

Approved for use in:

Locally advanced and/or metastatic breast cancer

Dosage:

Drug	Dose	Route	Frequency
Epirubicin	**20mg/m^2**	IV	Every 7 days

Dose can be escalated to 30mg/m^2 if well tolerated

Repeat weekly whilst clinically effective.

At 18 weeks review clinically and **ensure maximum cumulative dose not reached**.

Continue if ongoing benefit from treatment.

NOTE:

Maximum cumulative dose of epirubicin: 720 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%**

Risk factors for cardiac toxicity include active or dormant cardiovascular disease, prior or **concomitant radiotherapy to the mediastinal/pericardial area**, previous therapy with other anthracyclines or anthracenediones, concomitant use of other drugs with the ability to

suppress cardiac contractility or cardiotoxic drugs (e.g., trastuzumab) with an increased risk in the elderly.

Emetogenic risk:

Moderately emetogenic.

Supportive treatments:

Metoclopramide 10mg oral tablets, up to 3 times a day or as required for a maximum of 5 consecutive days.

Extravasation risk:

Vesicant - Refer to the CCC policy for the 'Prevention and Management of Extravasation Injuries'

Dosing in renal and hepatic impairment:

Renal	No dose adjustments needed

Hepatic	**Bilirubin (µmol/L)**		**AST**	**Epirubicin dose**	
	21 to 51	OR	2-4 x ULN	50%	
	52 to 86	OR	>4x ULN	25%	
	Above 86	OR	Child-Pugh C	omit	

Interactions:

Please refer to SmPC for full list of interactions.

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
1	**Dexamethasone**	**8mg**	**PO**	30 minutes before chemotherapy
	Ondansetron	**16mg**	**PO**	30 minutes before chemotherapy
	Epirubicin	**20mg/m^2**	**IV**	IV bolus over 10 to 15 minutes

				Concurrent administration, epirubicin at 400mL/hr and sodium chloride 0.9% at 100mL/hr

Main toxicities:

Haematological	Neutropenia, anaemia, thrombocytopenia,
Cardiac and Vascular disorders	Cardiomyopathy, arrhythmias
Gastrointestinal	Nausea, vomiting, diarrhoea, constipation, mucositis
Hepatobiliary	Elevation of liver transaminases, alkaline phosphatase and bilirubin.
Skin and subcutaneous tissue disorders	Alopecia Phlebitis
General disorders and administration site conditions	Fatigue Infertility, early menopause

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Informed Consent	x				
Clinical Assessment	x			x	As clinically indicated or at the end of treatment
SACT Assessment (to include PS and toxicities)	x	x	x	x	Every cycle
FBC	x	x	x	x	Every cycle
U&E & LFTs & Magnesium	x	x	x	x	Every Cycle
CrCl (Cockcroft and Gault)	x	x	x	X	Every cycle
CT scan	x				Every 8 weeks and repeats as clinically indicated
ECG					If clinically indicated
ECHO/MUGA	x				And repeat if clinically indicated
Full set of observations	x	x	x	x	Every cycle
Weight recorded	x	x	x	x	Every cycle
Height	x				

Dose Modifications and Toxicity Management:

Haematological toxicity:

Proceed on day 1 if-

ANC ≥ 1.0 x 10^9/L	Plt ≥ 100 x 10^9/L

Delay 1 week on day 1 if-

ANC ≤ 0.9 x 10^9/L	Plt ≤ 99 x 10^9/L

If bone marrow infiltration then these limits may be adjusted by the Consultant Oncologist

Non- Haematological toxicity:

Cardiomyopathy	Perform baseline MUGA in any patient with suspected cardiac impairment. If cardiac ejection fraction < 50% discuss with consultant and consider an alternative regimen. The risk of developing Congestive Heart Failure (CHF) increases rapidly with increasing total cumulative doses of epirubicin hydrochloride in excess of 900 mg/m2; this cumulative dose should only be **exceeded with extreme caution.** Consider a lower maximum cumulative epirubicin dose ≤ 900mg/m^2 for any patient with cardiac dysfunction or that has been exposed to mediastinal radiation Note that cardiomyopathy may be delayed – if 20% reduction if LVEF after 600mg/m^2 then stop epirubicin

References:

1. Epirubicin Hydrochloride 2 mg/ml solution for injection or infusion SmPC, Accord Healthcare Ltd accessed via https://www.medicines.org.uk/emc. Last updated 24 Apr 2019.

2. Supplement to: Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20: e201–08.
3. Twelves et al Br J Cancer 1989 60(6):938-941
4. Gasparini et al Am J Clin Oncol 1991 14(1):38-44

Circulation/Dissemination

Date added into Q-Pulse	2nd February 2023
Date document posted on the Intranet	N/A

Version History

Date	Version	Author name and designation	Summary of main changes
		Helen Flint	New regimen protocol V1.0
October 2022	1.1	**Gabriella Langton**	**Routine protocol update** **V1.1**