SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Eribulin
Advanced Breast Cancer

PROTOCOL REF: MPHAERIBBR
(Version No. 2.1)

Approved for use in:

Locally advanced or metastatic breast cancer, when the cancer has progressed after at least 1 prior chemotherapy regimen for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting unless patients were not suitable for these treatments.

*********BLUETEQ REGISTRATION REQUIRED**********

Dosage:

Drug	Dose	Route	Frequency	Duration
ERIBULIN	**1.23 mg/m^2**	IV infusion	Day 1 and 8 of a 21 day cycle	Treatment continues until disease progression or unacceptable toxicity

Emetogenic risk:

Low emetogenic risk

Supportive treatments:

Metoclopramide 10mg tablets to be taken three times a day when required.

Extravasation risk:

Non-vesicant

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

Dosing in renal and hepatic impairment:

Renal	>50ml/min	No dose adjustment necessary
	<50ml/min	75% of the original dose

Hepatic

Hepatic Impairment	**Recommended Dose**
Mild (Child-Pugh A)*	0.97mg/m^2 (75% dose reduction)
Moderate (Child-Pugh B)*	0.62 mg/m^2 (50% dose reduction)
Severe (Child-Pugh C)*	No formal studies- a more marked dose reduction is required.

Patients with ALT or AST > 3 x ULN and/or bilirubin > 1.5 x ULN have increased risk of toxicity. If LFTs increase to these levels during treatment then withhold and refer back to oncologist for review.

Consider starting dose of 0.97mg/m^2 (75%) in patients with impaired liver function at baseline, bilirubin between ULN and 1.5 x ULN. If bilirubin above 1.5 x ULN prior to cycle 1 then start at lowest dose level of 0.62mg/m^2

*Assessing a Child-Pugh score (for an adult patient)

Parameters	1 point	2 points	3 points
Total bilirubin (µmol/L)	< 34	34–50	> 50
Serum albumin (g/L)	> 35	28–35	< 28
Prothrombin time, prolongation (s) *Or* INR	< 4 < 1.7	4–6 1.7-2.3	> 6 >2.3
Ascites	None	Mild to Moderate (diuretic responsive)	Severe (diuretic refractory)
Hepatic encephalopathy	None	Grade I–II (or suppressed with medication)	Grade III–IV (or refractory to medication)

Child-Pugh Class
A (5-6 points)
B (7-9 points)
C (10 or more points)

INR: International Normalised Ratio.
Please note: assessment of Child-Pugh Class is to help guide clinical teams when prescribing and pharmacists when screening.

Interactions:

Avoid concomitant treatment with enzyme inducing drugs such as carbamazepine, phenytoin and St John's wort, as these are likely to give markedly reduced plasma concentrations of eribulin.

Low magnesium and low potassium should be corrected before starting treatment (As eribulin can cause QT prolongation).

Please refer to the SmPC for full list of drug interactions.

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
1 and 8	Dexamethasone	8mg	PO	30 minutes before chemotherapy
	Eribulin	**1.23mg/m^2**	IV	In 100mL sodium chloride 0.9% over 15 minutes

Do not administer through an intravenous line containing solutions with glucose

Main toxicities:

Haematological	Neutropenia, anaemia, thrombocytopenia,
Gastrointestinal	Nausea, vomiting, diarrhoea, constipation, mucositis
Musculoskeletal	Arthralgia, myalgia
Nervous system	Peripheral neuropathy, headache
Hepatobiliary	Elevation of liver transaminases, alkaline phosphatase and bilirubin.
Skin and subcutaneous tissue disorders	Alopecia
General disorders and administration site conditions	Fatigue Infertility, early menopause

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 1 D8	Cycle 2	Cycle 2 D8	Cycle 3	Cycle 3 D8	Ongoing
Informed Consent	X							
Clinical Assessment	X					X		As clinically indicated
SACT Assessment (to include PS and toxicities)	X	X	X	X	X	X	X	Every cycle
On treatment review	X	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	X	Every cycle
U&E & LFTs & Magnesium	X	X	X	X	X	X	X	Every cycle
CT scan	X							Every 12 weeks or as clinically indicated
Blood pressure measurement	X							Repeat if clinically indicated
Weight recorded	X	X	X	X	X	X	X	Every cycle
Height recorded	X							

Dose Modifications and Toxicity Management:

Haematological toxicity:

Cycle 1 ONLY:

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ANC ≥ 1.5 x 10^9/L	Platelets ≥ 100 x 10^9/L

Subsequent cycles:

Proceed on day 1 and 8 if-

ANC ≥ 1.0 x 10^9/L	Plat ≥ 75 x 10^9/L

Delay 1 week on day 1 and 8 if:

ANC ≤ 0.9 x 10^9/L	Platelets ≤ 74 x 10^9/L

Or

Any Grade 3 or 4 non-hematological toxicities (refer to dose reduction recommendations below).

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.

Non- Haematological toxicity:

Neuropathy: If any grade 2 or 3 neuropathy in the previous cycle withhold until recovered to grade 1, then reduce the eribulin dose to 0.97mg/m^2 (75%) on day 1 and day 8.

If there is any recurrence despite the dose reduction, reduce the dose further to 0.62mg/m^2 (50%). Consider discontinuing treatment if any further recurrence despite this second dose reduction.

Other Non-haematological toxicities: If any other grade 3 or 4 toxicities in the previous cycle, reduce the eribulin dose to 0.97mg/m^2 (75%) on day 1 and day 8.

If there is any recurrence despite the dose reduction, reduce the dose further to 0.62mg/m^2. Consider discontinuing treatment if any further recurrence despite this second dose
reduction.

Adverse reaction after previous eribulin administration	**Recommended dose of eribulin**
Haematological:	
ANC < 0.5 x 10^9/l lasting more than 7 days	0.97 mg/m^2 (75%)
ANC < 1 x 10^9/l neutropenia complicated by fever or infection	
Platelets < 25 x 10^9/l thrombocytopenia	
Platelets < 50 x 10^9/l thrombocytopenia complicated by haemorrhage or requiring blood or platelet transfusion	
Non-haematological:	
Any Grade 3 or 4 in the previous cycle	
Reoccurrence of any haematological or non-haematological adverse reactions as specified above	
Despite reduction to 0.97 mg/m^2	0.62 mg/m^2 (50%)
Despite reduction to 0.62 mg/m^2	Consider discontinuation

The dose of eribulin should not be re-escalated after it has been reduced.

Please note:

In the EU the recommended dose refers to the base of the active substance (eribulin). Calculation of the individual dose to be administered to a patient must be based on the strength of the ready to use solution that contains 0.44 mg/ml eribulin and the dose

recommendation of 1.23 mg/m^2. The dose reduction recommendations shown below are also shown as the dose of eribulin to be administered based on the strength of the ready to use solution.

In the pivotal trials, the corresponding publications and in some other regions e.g. the United States and Switzerland, the recommended dose is based on the salt form (eribulin mesilate).

References:

1. Eribulin SPC https://www.medicines.org.uk/emc/product/4517/smpc
2. 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. BNF available via: https://bnf.nice.org.uk/drugs/eribulin/
4. NICE: TA423. Eribulin for treating locally advanced or metastatic breast cancer after 2 or more chemotherapy regimens. https://www.nice.org.uk/guidance/ta423
5. Cortes et al Lancet 2011 Mar 12 377(9769):914-23. Eribulin monotherapy versus treatment of physician's choice in patients with metastatic breast cancer (EMBRACE): a phase 3 open-label randomised study
6. Macpherson IR et al Breast Cancer Research 2021 23: 33 (2021): 2256 Eribulin, Child-Pugh score and liver function tests: lessons from pivotal breast cancer studies 301 and 305

Circulation/Dissemination

Date added into Q-Pulse	7th September 2023
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Version History

Date	Version	Author name and designation	Summary of main changes
June 2023	V2.1	**Gabriella Langton, Advanced Pharmacist**	Updated to new format, updated hepatic information and dose reductions