Systemic Anti Cancer Treatment Protocol

Eribulin
Advanced Breast Cancer

PROTOCOL REF: MPHAERIBBR
(Version No: 1.0)

Approved for use in:

Locally advanced or metastatic breast cancer, when the cancer has progressed after at least 2 chemotherapy regimens (which may include an anthracycline or a taxane, and capecitabine)

Requires blueteq registration

Dosage:

Drug	Dosage	Route	Frequency
Eribulin	1.23mg/m^2	IV	Day 1 and 8 of 21 day cycle

Treatment continues until disease progression or unacceptable toxicity

Supportive treatments:

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

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).

Extravasation risk

Non-vesicant

Administration:

Day	Drug	Dose	Route	Diluent and rate
1 and 8	Dexamethasone	8mg	PO	30 minutes before chemotherapy
1 and 8	**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:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Medical Assessment	X		X		X	Alternate cycles
Nursing Assessment		X	X	X	X	Every cycle
FBC	X		X	X	X	Every cycle
U&E & LFT	X		X	X	X	Every cycle
CT scan	X					Every 8 to 12 weeks as clinically indicated
Informed Consent	X					
PS recorded	X	X	X	X	X	Every cycle
Toxicities documented	X		X	X	X	
Weight recorded	X	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if:-

Platelets ≥ 75 x 10^9/L	ANC ≥ 1.0 x 10^9/L

Delay 1 week on day 1 if:-

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

Parameter	**Recommended dose at 1st occurrence**
ANC < 0.5 x 10^9/L lasting more than 7 days	0.97mg/m^2
ANC < 1.0 x 10^9/L neutropenia complicated by fever or infection	0.97mg/m^2
Platelets < 25 x 10^9/L	0.97mg/m^2
Platelets < 50 x 10^9/L complicated by haemorrhage or requiring blood or platelet transfusion	0.97mg/m^2

If subsequent episodes than dose reduce to 0.62mg/m^2

Non-haematological toxicity

Renal function: For patients with mild or moderate hepatic and/or moderate (CrCl 30-50 mL/min) renal impairment, a reduction in starting dose is recommended.

Avoid in moderate to severe renal failure, e.g. CrCl < 30mL/min

Hepatic Function: Avoid in moderate to severe impaired hepatic function.

Patients with ALT or AST greater than 3 times ULN and/or bilirubin greater than 1.5 times 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 in patients with impaired liver function at baseline

For Child Pugh A reduce starting dose to 0.97mg/m^2

For Child Pugh B reduce starting dose to 0.63mg/m^2

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

Parameter	Score		
	1	2	3
Ascites	None	Mild to moderate Easily treated	Moderate to severe
Encephalopathy	None	Grade 1 to 2	Grade 3 to 4
Bilirubin (micromol/L)	< 35	35 to 50	< 50
Albumin (g/L)	35	28 to 35	< 28
INR	< 1.7	1.8 to 2.3	> 2.3

Child Pugh score 5 to 6 = Grade A; well-functioning liver

Child Pugh score 7 to 9 = Grade B; significant functional compromise

Child Pugh score 10 to 15 = Grade C; decompensate liver

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 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.

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 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.

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:

Eribulin SPC

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EMBRACE: Eribulin monotherapy in metastatic breast cancer
Cortes et al Lancet 2011 Mar 12 377(9769):914-23

Drugs and the Liver, Edited by Penny North Lewis
Pharmaceutical Press 2008