

PMitCEBO

Non Hodgkins Lymphoma

Salvage therapy, particularly for patients aged > 60 years

Drugs/Dosage:	Mitoxantrone	7mg/m ²	IV	D1
	Cyclophosphamide	300mg/m ²	IV	D1
	Etoposide	150mg/m ²	IV	D1
	Vincristine	1.4mg/m ² (max 2mg)	IV	D8
	Bleomycin	10,000iu/m ²	IV	D8
	Prednisolone	50mg po once daily on weeks 1 – 4, then 50mg po on alternate days from week 5 to end of treatment		
Administration:	Vincristine and Mitoxantrone via fast running infusion of 0.9% Sodium Chloride Etoposide in 500 – 1000ml 0.9% Sodium Chloride over 1 hour Bleomycin in 100 ml 0.9% Sodium Chloride over 15 minutes or slow bolus via fast running infusion of 0.9% Sodium Chloride Cyclophosphamide may be given as a bolus			
Other drugs:	Allopurinol 300mg po daily – review after 2 weeks Use of proton pump inhibitor or H ₂ receptor antagonist (e.g. ranitidine) is recommended whilst treating with steroids.			
Frequency:	2 weekly cycle for 6 - 8 cycles Treat to CR or non-progressive PR plus a further 4 weeks of chemotherapy			
Main Toxicities:	myelosuppression; alopecia; mucositis; cardiomyopathy (see Comments); peripheral neuropathy; constipation; skin reactions to bleomycin; pulmonary toxicity; steroid side effects; rigors with bleomycin (see Comments); ovarian failure; infertility			
Anti – emetics:	highly emetogenic – D1 (but oral dexamethasone not needed due to prednisolone) mildly emetogenic – D8			
Extravasation:	Vincristine is a vesicant			
Regular Investigations:	FBC	D1 & D8 for 1 st 2 cycles, then review need for D8		
	LFTs	D1 of alternate courses		
	U&Es	D1 of alternate courses		
	LDH	D1 of alternate courses		
	MUGA/echo	see Comments		
	CXR and lung function tests	baseline and according to local practice (see Comments)		
Comments:	Maximum cumulative dose of mitoxantrone = 160mg/m ² A baseline MUGA scan/echo should be performed where the patient is considered at risk of having impaired cardiac function e.g. significant cardiac history, hypertension, obese, smoker, elderly, previous exposure to anthracyclines, previous			

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thoracic radiotherapy. MUGA/echo should be repeated if there is suspicion of cardiac toxicity at any point during treatment, or if cumulative dose of mitoxantrone and any previous anthracyclines approaches maximum.

If pyrexial reaction to bleomycin occurs despite presence of oral prednisolone, give dexamethasone 4mg IV before each dose.

Bleomycin pulmonary toxicity is age-dependent, with an increase in frequency and associated mortality as patient age rises above 40 years. Dose modifications for bleomycin should be made according to table below. Bleomycin should be used with caution if approaching maximum cumulative dose. Baseline CXR and lung function tests are required, with lung function then closely monitored throughout treatment, according to local practice. There should be a low threshold for omitting further bleomycin if clinical concerns develop.

Age (years)	Maximum Bleomycin Dose per Week (IU)	Maximum Cumulative Dose (IU)
< 60	30,000 – 60,000	500,000
60 – 69	30,000 – 60,000	200,000 – 300,000
70 – 79	30,000	150,000 – 200,000
80 and over	15,000	100,000

Dose Modifications

Haematological Toxicity: If neutrophils $< 1.0 \times 10^9/l$ or platelets $< 100 \times 10^9/l$ on D1, delay chemotherapy until FBC recovered.
If low counts are thought to be due to marrow infiltration, discuss with Consultant.

Renal Impairment: If serum creatinine above normal range, estimate creatinine clearance using Cockcroft & Gault and dose cyclophosphamide accordingly.

CrCl (ml/min)	Cyclophosphamide Dose	Bleomycin Dose
> 50	Give 100%	Give 100%
10 – 50	Give 75%	Give 75%
< 10	Give 50%	Give 50%

CrCl (ml/min)	Etoposide Dose
60	Give 85%
45	Give 80%
30	Give 75%

Hepatic Impairment: Mitoxantrone is not recommended with severe hepatic insufficiency or if bilirubin $> 60\mu\text{mol/l}$. If in doubt, discuss with Consultant

Bilirubin ($\mu\text{mol/l}$)	ALT / AST (units/l)	Vincristine Dose
26 – 51 or	60 – 180	Give 50%
> 51 and	Normal	Give 50%
> 51 and	> 180	Omit

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Creatinine clearance is the strongest predictor of etoposide clearance. There is conflicting information about dose reduction with hepatic impairment. Use the table below, but discuss with Consultant before any dose reductions are made.

Bilirubin (μmol/l)	AST (units/l)	Etoposide Dose
26 – 51 or	60 - 180	Give 50% dose
> 51 or	> 180	Clinical decision

Neurotoxicity: Give 50% vincristine dose if Grade 2 motor and/or Grade 3 sensory toxicity
If in doubt, discuss with Consultant.

Lung Toxicity: Bleomycin must be discontinued permanently if any symptoms of lung toxicity

Skin Toxicity: Severe skin lesions eg desquamation, may require discontinuation of bleomycin

Patient Information: CancerBACUP leaflet for PMitCEBO

Reference: RMH / BNLI 60+ Trial (1997)

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