R-CHOP

CD20 positive Diffuse Large B-Cell Non-Hodgkins Lymphoma, Stage II, III or IV (NICE approved 2003)
N.B. Rituximab with any other combination of chemotherapy is not NICE approved for DLBC NHL

Drugs/Dosage:	**Rituximab**	375mg/m^2	IV	D1
	then			
	Cyclophosphamide	750mg/m^2	IV	D1
	Doxorubicin	50mg/m^2	IV	D1
	Vincristine	1.4mg/m^2 (max 2mg)	IV	D1
	Prednisolone	100mg (flat dose)	po daily	D1 to D5

Age > 60 yrs and pre-existing constipation or neurological problems, consider vincristine dose of 1mg. If in doubt, check with Consultant.

Premedication:	Paracetamol 1000mg po	60 minutes pre rituximab
	Chlorphenamine 10mg IV	15 minutes pre rituximab
	Dexamethasone 8mg or Hydrocortisone 100mg IV	15 minutes pre rituximab

Other drugs: Allopurinol 300mg po daily, starting at least 24 hours before first dose – review after 3 weeks
Use of proton pump inhibitor or H_2 receptor antagonist (eg ranitidine) is recommended whilst treating with steroids

Administration: Rituximab should be given before CHOP, diluted in 0.9% Sodium Chloride & administered according to following instructions:

First infusion: start at 50mg/hr; escalate in 50mg/hr increments every 30 minutes to a maximum of 400mg/hr

Subsequent infusions: if no problems with first infusion, start at 100mg/hr; escalate in 100mg/hr increments every 30 minutes to a maximum of 400mg/hr
if reactions occurred with first infusion, give second infusion as for first infusion

If reactions occur at any time, stop infusion. If symptoms improve, restart at 50% dose and accelerate as tolerated.

Doxorubicin & Vincristine via fast running infusion of 0.9% Sodium Chloride
Cyclophosphamide may be given as a bolus

Frequency: 3 weekly cycle for 8 cycles

Main Toxicities: severe cytokine release syndrome – usually occurs within 1–2 hours of the first rituximab infusion (see Comments); myelosuppression; alopecia; mucositis; cardiomyopathy; peripheral neuropathy; constipation; haemorrhagic cystitis; ovarian failure; infertility;
tumour lysis syndrome (ensure pre-medicated with allopurinol and good hydration)

Reason for Update: "wherever possible" removed from "rituximab should be given before CHOP" statement	Approved by Chair of Network TSSG: Dr A Laurie
Version: 3	Date: 10/11/06
Supersedes: Version 2	Review Date: February 2009
Prepared by: S Taylor	Checked by Network Pharmacist: Dermot Ball

Anti- emetics:	highly emetogenic (but oral dexamethasone not needed due to prednisolone)	
Extravasation:	Doxorubicin & Vincristine are vesicants	
Regular Investigations:	FBC	D1
	LFTs & U&Es	D1
	LDH	D1
	MUGA/echocardiogram	see Comments

Comments: Maximum cumulative dose of doxorubicin = 450 - 550mg/m^2

A baseline MUGA scan/echocardiogram should be performed where the patient is considered at risk of having impaired cardiac function e.g. significant cardiac history, hypertension, gross or morbid obesity, smoker, ≥ 70 years old, previous exposure to anthracyclines, previous thoracic radiotherapy. MUGA/echo should be repeated if there is suspicion of cardiac toxicity at any point during treatment.

Omit rituximab if WBC > 25 x 10^9/l, as increased risk of severe cytokine release syndrome. If in doubt, check with Consultant.

Full resuscitation equipment must be available, with immediate access to clinical staff trained in resuscitation for the first hour of the first rituximab infusion. Blood pressure, pulse and respiration must be measured and recorded every 15 minutes for the first hour of the first infusion.

Dose Modifications

Haematological Toxicity: If neutrophils < 1.0 x 10^9/l or platelets < 100 x 10^9/l on D1, proceed as follows:

Curative intent: discuss with Consultant re: delay/use of G-CSF to maintain dose intensity
Without curative intent: delay chemotherapy until FBC recovered, then continue with 20% dose reduction of doxorubicin and cyclophosphamide

If low counts are 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
> 50	Give 100%
10 – 50	Give 75%
< 10	Give 50%

Hepatic Impairment:

Bilirubin (µmol/l)	Doxorubicin Dose
20 – 50	Give 50%
51 – 85	Give 25%
> 85	Omit

Bilirubin (µmol/l)		ALT / AST (units/l)	Vincristine Dose
26 – 51	**or**	60 – 180	Give 50%
> 51	**and**	Normal	Give 50%
> 51	**and**	> 180	Omit

Neurotoxicity: Curative intent: Stop vincristine if patient experiences Grade 3 – 4 toxicity.
Without curative intent: Give 50% vincristine dose if Grade 2 motor and/or Grade 3 sensory toxicity
If in doubt, discuss with Consultant.

Patient Information: CancerBACKUP leaflets for CHOP and Rituximab

References:
Sonneveld, P et al (1995); JCO (13): 2530-2539
Blood 96:138 (1) 16 Nov 2000
Blood 96:223(1) 16 Nov 2000
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