R-CHOP

CD20 positive Diffuse Large B-Cell Non-Hodgkin's Lymphoma
An option for patients with symptomatic Stage III or IV follicular lymphoma

Omit rituximab for patients with CD20 negative lymphomas, or allergy to rituximab

All patients should be screened for hepatitis B virus before starting treatment

Drugs/Dosage:				
	Rituximab	375mg/m^2 (dose 'banded' according to dosing table below)	IV	Day 1
	Cyclophosphamide	750mg/m^2	IV	Day 1
	Doxorubicin	50mg/m^2	IV	Day 1
	Vincristine	1.4mg/m^2 (max 2mg)	IV	Day 1
	Prednisolone	100mg (flat dose)	po daily	Day 1 to Day 5

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	IV	15 minutes pre rituximab

IV dexamethasone only may be omitted if Day 1 of oral prednisolone (100mg) taken at least 30 minutes before start of rituximab infusion

Other drugs: Allopurinol 300mg po daily, starting at least 24 hours before first dose – review after 3 weeks
Omeprazole 20mg od (or ranitidine) is recommended whilst treating with steroids
Primary G-CSF should be routinely administered to all patients with diffuse aggressive lymphoma **aged > 65** and being treated with curative CHOP or R-CHOP.

Administration: Rituximab should be given before chemotherapy, diluted in 500ml 0.9% sodium chloride & administered according to following instructions:

First infusion[#]: start at 50mg/hr, according to infusion table below; escalate in 50mg/hr increments every 30 minutes to a maximum of 400mg/hr.
Monitor patient's vital signs (blood pressure, pulse, temp and O_2 saturation) at baseline and then every 30 minutes (before each increase in infusion rate) until end of infusion.

	Infusion Rate (mg/hour)							
	50	100	150	200	250	300	350	400
Rituximab 'banded' dose	**Infusion Rate (ml/hour) for rituximab in 500ml volume only**							
450mg	55	111	166	222	277	333	388	444
500mg	50	100	150	200	250	300	350	400
600mg	42	83	125	167	208	250	292	333
700mg	36	71	107	143	178	214	250	286
800mg	31	62	94	125	156	187	219	250
900mg	28	56	83	111	139	167	194	222
1000mg	25	50	75	100	125	150	175	200
1100mg	23	45	68	90	114	136	159	182

Reason for Update: info on split dosing of rituximab added	Approved by Chair of Alliance TSSG: Dr A Laurie
Version: 13	Date: 22.8.16
Supersedes: Version 12	Review Date: Sept 2018
Prepared by: S Taylor	Checked by: C Tucker

Subsequent Infusions:

*** Patients who tolerated their first infusion at the standard recommended rate only ***
Give 20% of dose (i.e. 100ml) over 30 minutes, then the remaining 80% (i.e. 400ml) over 1 hour, to give a total infusion time of 90 minutes.
Monitor patient's vital signs at baseline, then every 30 minutes until end of infusion.

*** Patients who did not tolerate their first infusion at the standard rate ***
Administer and monitor as per first infusion, or at a slower rate if required.

#**If WBC ≥ 25 x 10^9/l,** there is an increased risk of severe cytokine release syndrome with rituximab administration. Options include omitting the rituximab for this cycle, or splitting rituximab dosing over two days, as follows:

Day 1: **rituximab 50mg/m²** in 50ml sodium chloride 0.9% IV infusion at 50mg/hr fixed rate throughout.
Day 2: **rituximab 325mg/m²** in 250-500ml sodium chloride 0.9% IV infusion, start at 50mg/hr, escalate in 50mg/hr increments every 30 mins to max 400mg/hr.

Full resuscitation equipment must be available, with immediate access to clinical staff trained in resuscitation for the first hour of the first rituximab infusion.

If reactions occur at any time, stop the infusion. If symptoms improve, restart at half the previous infusion rate, and escalate as tolerated.

Doxorubicin injection via fast running infusion of 0.9% sodium chloride
Vincristine diluted in 50ml 0.9% sodium chloride and infused over 5-10 minutes
Cyclophosphamide may be given as a bolus

Frequency:

3 weekly cycle
Stage IA DLBCL: 3 – 4 cycles, with IF radiotherapy
Stage II – IV DLBCL } Treat for a minimum of 6 cycles and a maximum of 8 cycles
Stage III – IV FL }

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)

Anti- emetics:

highly emetogenic (but antiemetic dexamethasone not needed due to prednisolone)

Extravasation:

Doxorubicin & vincristine are vesicants

Regular Investigations:

FBC	Day 1
LFTs & U&Es	Day 1
LDH	Day 1
MUGA/echocardiogram	see Comments

Comments:

Maximum cumulative dose of doxorubicin = 450 - 550mg/m²

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. If ejection fraction < 50%, omit the doxorubicin or use the R-GCVP regimen.
MUGA/echo should be repeated if there is suspicion of cardiac toxicity at any point during treatment.

Dose Modifications

Haematological Toxicity:

If neutrophils < 1.0 x 10^9/l or platelets < 100 x 10^9/l on Day 1, 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:

CrCl (ml/min)	Cyclophosphamide Dose
> 20	Give 100%
10 – 20	Give 75%
< 10	Give 50%

Hepatic Impairment:

ALT / AST		Bilirubin (µmol/l)	Doxorubicin Dose
2 – 3 x ULN		-	Give 75%
> 3 x ULN	**or**	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**	≤ 180	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: Macmillan leaflet for R-CHOP

References:

Sehn et al; Blood 2007; 109 (10): 4171 – 4173
NICE Technology Appraisal 65 (TA65)
NICE Technology Appraisal 243 (TA243)