R-mini-CHOP

[Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisolone*]

INDICATION

Licensed / NHSE funded: **NON-HODGKIN LYMPHOMA (NHL)** [ICD-10 codes: C82-86]

Treatment of patients with NHL, typically over the age of 80 years, or with significant co-morbidities

Omit rituximab if CD20-negative

* Prednisolone can be replaced with Dexamethasone in suspected or confirmed CNS disease.

TREATMENT INTENT

Curative or disease modification depending on clinical circumstances

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PRE-ASSESSMENT

1. Ensure histology is confirmed prior to administration of chemotherapy and document in notes.
2. Record stage and IPI of disease - CT scan (neck, chest, abdomen and pelvis), and/or PET-CT, presence or absence of B symptoms, clinical extent of disease. Consider bone marrow aspirate and trephine if clinically indicated.
3. Blood tests – FBC, U&Es, LDH, ESR, urate, calcium, vitamin D level, magnesium, creatinine, LFTs, glucose, HbA1c, Igs, β_2 microglobulin, hepatitis B core antibody and hepatitis B surface antigen, hepatitis C antibody, EBV, CMV, VZV, HIV, HTLV-1, glucose 6-phosphate dehydrogenase (G6PD) when indicated (refer to [H.8]); group and save.
4. Assess **glycaemic control** as steroids in this regimen can increase the risk of hyperglycaemia. All patients should have a baseline HbA1c and venous plasma glucose checked prior to commencing treatment, followed by venous plasma glucose checked at each cycle and antidiabetic medications managed according to local policies and the UK Chemotherapy Board and Joint British Diabetes Societies for Inpatient Care [JBDS-IP] guideline.
5. Urine pregnancy test - before cycle 1 of each new chemotherapy course for women of child-bearing age unless they are post-menopausal, have been sterilised or had a hysterectomy.
6. ECG +/- ECHO* (*usually required for patients > 80 years of age) and baseline BP in all patients with a cardiac history or at risk of cardiac complications (hypertension, smokers, diabetes).
7. Record performance status [ECOG].
8. Record vital signs, height and weight.
9. Consent and counselling – ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given. Obtain written consent on the day of treatment.
10. Fertility – it is very important the patient understands the potential risk of infertility. All patients should be offered fertility advice by referring to the Oxford Fertility Unit.
11. Assess and document tumour lysis risk as part of pre-assessment. Patients should be adequately hydrated before and after each cycle administration. Hydration – in patients with bulky disease pre-hydrate with sodium chloride 0.9% 1 liter over 4-6 hours. Refer to the Tumour Lysis Syndrome in Adults protocol [H.8].
12. Some older patients may benefit from a **steroid pre-phase** (for example, 7 days of oral prednisolone at a dose of 50-100 mg daily).
13. **Dexamethasone can be used instead of prednisolone** in this regimen for patients with confirmed or suspected central nervous system (CNS) disease or when otherwise indicated by the Consultant (see DRUG REGIMEN below).
14. Advise dental check is carried out by patient's own dental practitioner before treatment starts.
15. Treatment should be agreed in the relevant MDT.

DRUG REGIMEN

Day(s)	Drug	Dose	Route	Administration details
1	Paracetamol Chlorphenamine	1000 mg 10 mg	PO IV	≥ 30 minutes before rituximab
1–5	**PREDNISOLONE***	**40 mg/m² OD**	PO	Take in the morning with food [Day 1 ≥ 30 minutes before rituximab]
1	**RITUXIMAB**	**375 mg/m²**	IV	In 500mL sodium chloride 0.9% [Refer to [Nursing Care Plans: Rituximab infusion rates], max. rate 400mg/hour]. Patients should be observed for 30 minutes before the start of other infusions. If first dose well tolerated, consider rapid infusion rituximab rate from cycle(s) 2 onwards.
1	**DOXORUBICIN**	**25 mg/m²**	IV	Bolus injection
1	**VINCRISTINE**	**1 mg**	IV	In 50 mL sodium chloride 0.9% over 10 minutes
1	**CYCLOPHOSPHAMIDE**	**400 mg/m²**	IV	Bolus injection
CYCLE FREQUENCY: 21 days (patients with low grade NHL may need 28-day cycles)				
TREATMENT DURATION: 6 cycles				

* **Alternatively, dexamethasone can be used** instead of prednisolone at the Consultant discretion. The dexamethasone dose may vary, for example, 8-40 mg/day for 4-5 days.

CONCURRENT MEDICATIONS

TLS prophylaxis	Hydration + allopurinol 300mg daily (reduce dose in renal impairment) for 7 days or consider rasburicase if high risk TLS [Cycle 1]. Refer for full details to "Tumour Lysis Syndrome in Adults" protocol [H.8].
Antiviral prophylaxis	Aciclovir 200mg three times a day for duration of treatment and for 3 months after completion
Gastric protection	Omeprazole 20mg once a day on days 1–5
G-CSF prophylaxis	Filgrastim **0.5 MU/kg/day**, starting **from day 6** for 5 days
Anti-emetics Day 1: High risk	▪ Ondansetron on day 1: 8mg BD & day 2: 8mg OD ▪ Metoclopramide on days 1-4: 10-20mg TDS. For breakthrough nausea or vomiting: 10-20mg TDS when required. For alternative options, refer to [TVCA Anti-emetic guideline].
Vitamin D supplement*	If required: Vitamin D < 50 nmol/L: replace as per local formulary
Bone protection*	Refer to "Bone Protection in Lymphoma" supportive care guidance [L.132]
Hemorrhagic cystitis prophylaxis* (when required, for example, for patients with pre-existing bladder disorders)	Regimen 1: Mesna PO 160mg/m² (40% of IV cyclophosphamide dose), starting 2 hours before cyclophosphamide injection, 4-hourly for 3 doses. Regimen 2: Mesna IV 80mg/m² (20% of IV cyclophosphamide dose), immediately before cyclophosphamide injection, followed by mesna PO 160mg/m² (40% of IV cyclophosphamide dose) at 2 and 6 hours after the IV mesna dose. In patients at high risk of urothelial toxicity, a shorter interval may be left between mesna doses, the number of doses increased, or both.
PJP prophylaxis*	Consider in the post-transplant lymphoproliferative disorder (PTLD), or if another risk factor is present (e.g. immunosuppressive medication): Co-trimoxazole 480mg three times a week on Mon/Wed/Fri for duration of treatment and at least 3 months after completion. Pentamidine can be considered for patients who are intolerant or allergic to co-trimoxazole.

(*) indicates optional concurrent medications

CONTRAINDICATIONS

Hypersensitivity to active ingredients and excipients. Active severe infections. Refer for full details to individual medications Summary of Product Characteristics (SmPCs).

INVESTIGATIONS

Before each cycle: FBC, U&Es, creatinine, LFTs, glucose, bone profile.
When clinically indicated: neurological examination, ECG.

RESTAGING

- Give 3-4 cycles and restage with CT (not required if disease is clinically assessable).
- If progressive or stable disease, consider other treatment.
- If partial or complete remission, continue up to 6 cycles.

DOSE MODIFICATIONS

Discuss dose reductions with the Consultant.

Hematological toxicities – on the day of treatment		
Neutrophils [x 10^9/L]	≥ 1	Procced with 100% doses
	0.5 – < 1	If patient is fit and well, proceed with 100% doses If patient is unwell, delay by 1 week
	< 0.5	Delay by 1 week
Platelets [x 10^9/L]	≥ 75	Proceed with 100% doses
	50 – 74	Give 75% doses of cyclophosphamide and doxorubicin
	< 50	Delay by 1 week

Neuropathy	
Vincristine	In the presence of motor weakness or severe sensory symptoms, discuss reducing or withholding vincristine with the Consultant.

Cardiotoxicity	
Doxorubicin	▪ Consider doxorubicin cardiotoxicity and maximum lifetime anthracycline exposure. Doxorubicin must be used with caution, if at all, in patients with cardiac dysfunction (consider dose reductions). Discuss with the Consultant. ▪ **Recommended total maximum cumulative dose of doxorubicin** (additive to other anthracyclines): 450mg/m^2 (in normal cardiac function) or 400mg/m^2 (in cardiac dysfunction, age > 70 years or exposure to mediastinal irradiation).

Haemorrhagic cystitis	
Cyclophos-phamide	▪ If gross hematuria develops, cyclophosphamide should be withheld until resolution of cystitis and mesna treatment commenced as per SmPC. ▪ Cyclophosphamide dose reduction by 50% may be considered at the next cycle – discuss with the Consultant. Re-escalation of cyclophosphamide to the initial full dose is recommended if symptoms do not recur.

Tumour lysis syndrome (TLS) Grade 3 or 4
Following complete resolution of TLS, treatment may be restarted at the full/current doses during the next scheduled cycle in conjunction with prophylactic therapy.

Renal impairment	
Doxorubicin	GFR ≥ 10 mL/min: 100% dose GFR < 10 mL/min: no need for dose adjustment is expected
Vincristine	No need for dose adjustment is expected
Cyclophosphamide	GFR ≥ 30 mL/min: 100% dose GFR 10-29 mL/min: 75% dose GFR < 10 mL/min: omit or consider 50% dose at the Consultant discretion

Hepatic impairment	
Doxorubicin	Bilirubin < 20 µmol/L: 100% dose Bilirubin 20–50 µmol/L: 50% dose Bilirubin 51–86 µmol/L: 25% dose Bilirubin > 86 µmol/L or Child-Pugh C: omit
Vincristine	Bilirubin > 51 µmol/l: 50% dose
Cyclophosphamide	Mild and moderate: no need for dose adjustment is expected Severe: not recommended due to risk of reduced efficacy

DRUG INTERACTIONS

CYP3A4 and P-gp inhibitors	Increased risk of doxorubicin, vincristine and cyclophosphamide toxicities; when used concurrently, use with caution and monitor closely.
CYP3A4 inducers	Doxorubicin, vincristine and cyclophosphamide efficacy can be decreased; when used concurrently, use with caution and monitor closely.
Anti-diabetic medications	Steroids may increase blood glucose levels – monitor closely. Patients with diabetes mellitus receiving concurrent insulin and/or oral hypoglycaemic agents may require dosage adjustments.
Anti-hypertensive medications	Since hypotension may occur during rituximab administration, consider withholding anti-hypertensive medication(s) 12 hours prior to the rituximab infusion.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

- Neutropenia and febrile neutropenia – primary prophylaxis with G-CSF is recommended.
- Alopecia
- Nausea and vomiting – prophylaxis with anti-emetics is recommended.
- Cyclophosphamide may irritate the bladder mucosa. Patients should be encouraged to drink a minimum of three litres of fluid per 24 hours.
- Cardiotoxicity - monitor cardiac function. Doxorubicin may be stopped in future cycles if signs of cardiotoxicity, e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.
- Vincristine may cause neurotoxicity. It is for intravenous use only; fatal if given by other routes.
- Rituximab may cause patient chillness, fever, headache, tiredness, aching muscles and joints, itching redness of skin, nausea and mild drop in blood pressure.
- Hepatitis B reactivation – following rituximab administration – see pathway for treatment and management of HBV positive patient [LPW.21].
- Steroid-related side effects may include osteoporosis, hyperglycaemia, hypertension, eye disorders, hypokalaemia, susceptibility to infection, gastrointestinal side-effects (peptic ulceration, indigestion), thinning of the skin - monitor BMs, BP, electrolytes; use with caution in patients with co-morbidities, e.g., diabetes, cardiovascular diseases, glaucoma.

EXTRAVASATION RISK

Rituximab: neutral
Cyclophosphamide: neutral
Doxorubicin: vesicant
Vincristine: vesicant

TREATMENT RELATED MORTALITY

1-5%

REFERENCES

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CORRESPONDING DOCUMENTS

R-mini-CHOP Nursing Care Plan [N-L.83]

REVIEW

Name	Revision	Date	Version	Review date
Cheuk-kie Jackie Cheung, Haematology Pharmacist	Cycle frequency section updated with IPI scores	July 2017	1.1	
	Removal of fluconazole	May 2018	1.2	
NSSG Lymphoma Group	Annual protocol review	May 2019	1.3	
Cheuk-kie Jackie Cheung, Haematology Pharmacist	Addition of PTLD as PCP prophylaxis consideration	Sep 2019	1.4	May 2021
Quality manager	Addition of nursing care plan	Oct 2020	1.5	May 2021
Sara Castro, Advanced Haematology Pharmacist	Annual protocol review	April 2021	1.6	
NSSG Lymphoma Group	Annual protocol review	July 2023	2.0	July 2025
Natalia Czub, Advanced Haematology Pharmacist, Dr Graham Collins, Consultant Haematologist; NSSG Lymphoma & CLL Group	Pre-assessment [glycaemic control advice added]. Drug regimen [dexamethasone included as alternative to prednisolone]. Concurrent medications [anti-emetics included; G-CSF duration updated]. Dose modifications updated. Link to R-mini-CHOP Nursing Care Plan as corresponding document. General formatting. Annual protocol review.	September 2024	2.1	September 2026