

Chlorambucil +/- R

INDICATION

Low-grade non-Hodgkin lymphomas (NHL) and other lymphoproliferative disorders including relapsed chronic lymphocytic leukaemia (CLL).

For CD20+ disease, consider use in combination with rituximab

TREATMENT INTENT

Disease modification.

PRE-ASSESSMENT

1. Ensure histology is confirmed prior to administration of chemotherapy and document in notes.
2. Record stage of disease – By clinical examination for CLL or by CT scan for NHL (neck, chest, abdomen and pelvis), presence or absence of B symptoms, clinical extent of disease, consider bone marrow aspirate and trephine.
3. Blood tests - FBC, DAT, U&Es, LDH, ESR, urate, calcium, magnesium, creatinine, LFTs, glucose, Igs, β_2 microglobulin, hepatitis B core antibody and hepatitis BsAg, hepatitis C antibody, EBV, CMV, VZV, HIV 1+2 after consent, group and save.
4. Urine pregnancy test - before cycle 1 of each new chemotherapy course in women of child-bearing age unless they are post-menopausal, have been sterilised or undergone a hysterectomy.
5. ECG +/- Echo - *if clinically indicated*.
6. Record performance status (WHO/ECOG).
7. Record height and weight.
8. Consent - 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.
9. 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.
10. Hydration - *in patients with bulky disease* pre-hydrate with sodium chloride 0.9% 1 litre over 4-6 hours. Patients at high risk of tumour lysis refer to tumour lysis protocol.
11. Consider dental assessment / Advise dental check is carried out by patient's own dental practitioner before treatment starts.
12. For patients prescribed oral chemotherapy, ensure pre-chemotherapy counselling in line with NPSA recommendation and chemotherapy measures.
13. Treatment should be agreed in the relevant MDT.

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DRUG REGIMEN**Days 1 to 14** CHLORAMBUCIL 10 mg daily PO

OR

Days 1 to 7 CHLORAMBUCIL 10 mg/m²/day

OR

Continuous CHLORAMBUCIL 4 mg daily PO

Tablets should be taken on an empty stomach (at least 1 hour before or 3 hours after meals).

RITUXIMAB dose is dependent on indications:For **CLL** patients**Day 1** **Pre-med** - paracetamol 1g PO, chlorphenamine 10 mg IV, hydrocortisone 100 mg IV 30 minutes before rituximab.**RITUXIMAB** 375 mg/m² IV infusion in 500 mL sodium chloride 0.9%. (cycle 1)**RITUXIMAB** 500 mg/m² IV infusion in 500 mL sodium chloride 0.9%. (cycles 2-6)Cycle 1: If lymphocyte count >25 x 10⁹/L:Give 50 mg/m² (or 100 mg flat dose) of Rituximab on day 1Give the rest (i.e. 325 mg/m²) on day 2Give 500 mg/m² on day 1 of subsequent cyclesFor **NHL** patients**Day 1** **Pre-med** - paracetamol 1g PO, chlorphenamine 10 mg IV, hydrocortisone 100 mg IV 30 minutes before rituximab.**RITUXIMAB** 375 mg/m² IV infusion in 500 mL sodium chloride 0.9%.**CYCLE FREQUENCY**

Every 28 days for 4-6 cycles (up to 12 cycles without R)

For single agent chlorambucil, stop 3 months following response plateau.

DOSE MODIFICATIONS**Haematological toxicity:** Treatment should be deferred if neutrophil count is <1.0 x 10⁹/L and/or if platelet count is <100 x 10⁹/L unless secondary to bone marrow infiltration.**Chlorambucil:**

Renal impairment	Hepatic impairment
No dose reduction required. Monitor myelosuppression	Dose reduce in patients with gross hepatic dysfunction. Modify dose according to response. Once the tolerance is established after the first month of therapy the dosage should be modified according to response, e.g. level of haematological suppression.

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INVESTIGATIONS

FBC, renal and liver profiles.

Clinical assessment at least every 3 months for patients on single agent chlorambucil.

CONCURRENT MEDICATION

Consider Allopurinol 300 mg daily for 7 days starting 24-48 hours prior to chemotherapy (first course / cycle only).

EMETIC RISK

Minimal to low.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Chlorambucil: Rash (well recognized complication usually widespread maculo-papular. Unusual if the patient is taking concomitant steroids.), involuntary movements, diarrhea, mouth ulcer and secondary haematologic malignancies.

Rituximab - severe cytokine release syndrome is characterised by severe dyspnoea, often accompanied by bronchospasm and hypoxia, in addition to fever, chills, rigors, urticaria, and angioedema. Hepatitis B reactivation.

EXTRAVASTATION RISK

Rituximab- neutral

TREATMENT RELATED MORTALITY

< 1%

REFERENCES

1. Aspen. Chlorambucil Summary of Product Characteristics. Updated 03/11/2015. Accessed 01/05/2018 via <http://www.medicines.org.uk/emc>
2. UCLH - Dosage Adjustment for Cytotoxics in Hepatic Impairment (Version 3 - updated January 2009).
3. UCLH - Dosage Adjustment for Cytotoxics in Renal Impairment (Version 3 - updated January 2009).

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