R-Chlorambucil

Indication
Treatment of follicular and other indolent lymphomas, Waldenström's macroglobulinaemia and chronic lymphocytic leukaemia.

ICD-10 codes
Codes with a prefix C81.

Regimen details

Day	Drug	Dose	Route
0 or 1	Rituximab*	375mg/m^2 (cycle 1) then 500mg/m2 for subsequent cycles (CLL)	IV infusion
1-14	Chlorambucil	10mg OD**	PO

* If appropriate for CD20+ disease
**Chlorambucil may be given at a continuous low dose of 2-4mg OD if concerns about tolerability.

If high tumour burden consider splitting the first dose of rituximab to give 50mg/m^2 (or 100mg) on day 0 and the remainder of the total dose on day 1.

Cycle frequency
Every 28 days

Number of cycles
Maximum 6 cycles

Administration
Rituximab is administered in 500mL sodium chloride 0.9%. The first infusion should be initiated at 50mg/hour and if tolerated the rate can be increased at 50mg/hour every 30 minutes to a maximum of 400mg/hour. Subsequent infusions should be initiated at 100 mg/hour and if tolerated increased at 100mg/hour increments every 30 minutes to a maximum of 400 mg/hour.

Chlorambucil is available as 2mg tablets. Tablets should be taken on an empty stomach, at least 1 hour before or 3 hours after a meal.

Pre-medication
Rituximab premedication:

- Paracetamol 500mg-1g PO 60 minutes prior to rituximab infusion
- Chlorphenamine 10mg IV bolus 15 minutes prior to rituximab infusion
- Dexamethasone 8mg IV bolus or hydrocortisone 100mg IV bolus 15 minutes prior to rituximab infusion

Consider pre-hydration for patients with bulky disease.

Emetogenicity
This regimen has mild-moderate emetogenic potential (days 1-14).

Additional supportive medication

Allopurinol 300mg (100mg if creatinine clearance <20mL/min) OD for the first cycle if required.
H_2 antagonist or PPI if required.
Antiviral and antifungal prophylaxis as per local policy.

Extravasation

Rituximab is neutral (Group 1)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days
LDH	14 days

Other pre-treatment investigations:
Hepatitis B and C and HIV serology

Investigations –pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	96 hours
U+E (including creatinine)	7 days
LFTs	7 days
LDH	7 days

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	**Limit**
Neutrophil count	≥ 1.0 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Creatinine clearance	≥ 45 mL/min
Bilirubin	≤ 1.5 x ULN
AST/ALT	< 2 ULN

Dose modifications

- **Haematological toxicity**

If neutrophils < 1.0 x 10^9/L **or** platelets < 100 x 10^9/L delay by 1 week or until count recovery. If counts recovered within 2 weeks resume at full dose, otherwise consider dose reduction.

- **Renal impairment**

No dose reduction usually required. If CrCl <45mL/min monitor closely for myelosuppression.

- **Hepatic impairment**

Chlorambucil should be dose reduced in severe hepatic impairment and the dose further modified based on response and degree of myelosuppression. Discuss with consultant if AST/ALT > 2 x ULN.

- **Other toxicities**

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Stevens-Johnson syndrome
Hypersensitivity and allergic reactions
Infertility

- **Frequently occurring side effects**

Nausea or vomiting
Anorexia, weight loss
Constipation, diarrhoea
Stomatitis/mucositis

- **Other side effects**

Rash

Significant drug interactions – for full details consult product literature/ reference texts

Coumarin-derived anticoagulants such as warfarin: patients established on warfarin should either be changed to low molecular weight heparin or have weekly monitoring of INR. Patients who are initiated on anti-coagulation should remain on low molecular weight heparin until completion of the course of chemotherapy.

Additional comments

Haematological toxicity may be cumulative.
Patients should receive irradiated blood products.

References

- Summary of Product Characteristics Rituximab (Roche). Accessed 12 October 2016 via www.medicines.org.uk
- Summary of Product Characteristics Chlorambucil (Medac). Accessed 12 October 2016 via www.medicines.org.uk
- MRC CLL4 Trial 2001
- Hillmen, P et al; Rituximab plus Chlorambucil as a first line treatment for CLL; JCO; 2014

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