Rituximab-Chlorambucil

INDICATION: Marginal Zone Lymphoma, CD20+ indolent lymphoma

Prior to a course of treatment:

- Ensure histology is confirmed prior to administration of chemotherapy and document in notes.
- Record stage of disease - CT scan (neck, chest, abdomen and pelvis), presence or absence of B symptoms, clinical extent of disease, bone marrow aspirate and trephine.
- 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.
- Urine pregnancy test - before cycle 1 of each new chemotherapy course in women aged 12 - 55 years of age unless they have been sterilised or undergone a hysterectomy.
- ECG +/- Echo - *if clinically indicated*.
- Record performance status (WHO/ECOG).
- Record height and weight.
- 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.
- Hydration - *in patients with bulky disease* pre-hydrate with sodium chloride 0.9% 1 litre over 4-6 hours. For patients at high risk of tumour lysis consider splitting the first dose of Rituximab as per local Rituximab policy and follow local guidance regarding prophylaxis/treatment of tumour lysis.
- Treatment should be agreed in the relevant MDT.

Prior to each dose

- Medical review of fitness for chemotherapy – exclude active infection, major changes in organ function
- Check FBC, U&Es, creat, LFTs - neuts must be >1.0 and plats > 100

Rituximab	**375mg/m2**	**IV infusion as per protocol****	**Day 1**
Chlorambucil*	**10mg/m2**	**PO**	**Days 1-7 (dividing the drug into 2-3 subdoses each day may improve tolerance)**

Repeat every 28 days for up to 12 cycles (rituximab with cycles 1-6 only)

* 2mg tablets Chlorambucil should be given after the rituximab infusion

Pre-infusion medications (approx. 1 hour prior)

- Paracetamol 1g PO
- Chlorphenamine 10mg IV
- Hydrocortisone 100mg IV (should be given prior to first 2 infusions. Hydrocortisone can then be omitted if no infusion reactions occur.)

**Give Rituximab infusion as per Trust Rituximab infusion policy. (This protocol is suitable for Rapid Infusion if the patient fulfils the criteria set in the Trust Rituximab policy).

Other medications

- Allopurinol 300mg daily for 28 days (100mg if Cr.Cl <20ml/min) for cycle 1 only
- Aciclovir 400mg BD prophylaxis throughout
- Co-trimoxazole 480 mg daily throughout
- Metoclopramide 10 mg TDS as required (emetic risk is minimal to low)

Dose modification for haematological toxicity (unless due to disease)	
• Day 28 neuts < 1.0 or plats <75	Delay treatment 1 week for up to 2 weeks (unless secondary to bone marrow infiltration)
• Neuts remain <0.5 or plats <50	Delay treatment until at least these levels reached with dose modification as necessary as below
• If counts do not recover to neuts >1.0, or plats > 75 despite delay	Proceed at 50% dose
Dose modification for liver dysfunction	
• Bilirubin > 57μmol/l	Consider initial dose reduction and adjust according to haematological toxicity
Dose modification for renal dysfunction	No initial reduction indicated but monitor carefully for haematological toxicity and adjust as necessary
If Creatinine Clearance is >50ml/min but>30ml/min,	Rituximab dose stays the same and chlorambucil dose can be reduced by 25%.
If Creatinine Clearance is <30ml/min but>10ml/min,	Chlorambucil dose can be reduced by 25%.
If Creatinine Clearance is <10ml/min ,	Chlorambucil dose can be reduced by 50%.

Toxicities

Rituximab toxicities

- Patients with high tumour burden or with a high number of circulating malignant cells are at risk of ***cytokine release syndrome***. This may manifest as severe dyspnoea, bronchospasm and hypoxia in addition to fever, chills, rigors, urticaria and angio-oedema (usually presents after 1 -2 hours of infusion). For patients who are at risk of tumour lysis syndrome, refer to tumour lysis protocol.
- PML (progressive multifocal encephalopathy),a rare demyelinating disease of the central nervous system that results from reactivation of latent JC polyoma virus (JCV), has been reported and should be considered in patients with new onset neurological symptoms or changes to pre-existing neurology. If suspected ask for neurology opinion
- Patients with chronic hepatitis B (HBsAg-positive) are at risk of viral reactivation if rituximab is administered without antiviral treatment, a potentially fatal complication of treatment**.** Patients with active hepatitis B disease should <u>not</u> be treated with rituximab. Patients with positive hepatitis B serology (either HBsAg or HBcAb) should be referred for a liver opinion and be monitored and managed to prevent hepatitis B reactivation.
- 10% of patients experience hypotension with the first dose of rituximab, therefore consideration should be given to withholding anti-hypertensive medications 12 hours prior to the rituximab Infusion. Hypotension with rituximab has been reported to occur 30 minutes to 2 hours after initiation of the infusion.

General Toxicities

Neutropenic sepsis & thrombocytopenia	Nausea & vomiting (none-mild)
Rash	Amenorrhoea & infertility (offer semen cryopreservation)
Mucositis	Potentially alopecia (mild)
Hepatotoxicity	Pulmonary fibrosis (late)
Second malignancies (late)	Fever, chills, hypotension, rigors & anaphylaxis (rituximab) – usually first dose only

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Date	July 2016
Review date	July 2018

References:

- HAEMATOLOGY CLINICAL GUIDELINES (LANCASHIRE & SOUTH CUMBRIA
- <u>Zucca et al. 2013 (IELSG-19)</u>