Chemotherapy Protocol

LYMPHOMA

RITUXIMAB SC

(12 weekly)

Regimen

- Lymphoma – Rituximab SC (12 weekly)

Indication

- Maintenance single agent therapy in relapsed / refractory follicular lymphoma, mantle cell lymphoma, marginal zone lymphoma and lymphoplasmacytic lymphoma in those who have responded to induction chemotherapy that has included intravenous rituximab

Toxicity

Drug	Adverse Effect
Rituxumab	Severe cytokine release syndrome, increased incidence of infective complications, progressive multifocal leukoencephalopathy, skin reactions

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- FBC, LFTs and U&Es prior to day one of treatment
- Consider monitoring serum immunoglobulin levels
- Check hepatitis B status before starting treatment with rituximab

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Each subcutaneous injection of rituximab should only be administered if the neutrophil count is at least $1x10^9$/L and the platelet count at least $75x10^9$/L.

Hepatic Impairment

Drug	Bilirubin µmol/L		AST/ALT units	Dose (% of original dose)
Rituximab	N/A		N/A	No dose adjustment needed

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Rituximab	N/A	No dose adjustment needed

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose should then be reduced to 75% of the original dose or discontinued as appropriate.

Rituximab

Infusion related adverse reactions have been observed in 10% of patients treated with rituximab.

Rituximab administration is associated with the onset of cytokine release syndrome. This condition is characterised by severe dyspnoea, often accompanied by bronchospasm and hypoxia, in addition to fever, chills, rigors, urticaria, and angioedema. It may be associated with some features of tumour lysis syndrome such as hyperuricaemia, hyperkalaemia, hypocalcaemia, acute renal failure, elevated lactate dehydrogenase (LDH) and can lead to acute respiratory failure and death. This effect on the lungs may be accompanied by events such as pulmonary interstitial infiltration or oedema, visible on a chest x-ray.

Cytokine release syndrome frequently occurs within one or two hours of initiating the first infusion.

Hypersensitivity reactions, including anaphylaxis, have been reported following the intravenous administration of proteins. In contrast to cytokine release syndrome, true hypersensitivity reactions typically occur within minutes of starting the infusion. Medicinal products for the treatment of allergic reactions should be available for immediate use in the event of hypersensitivity developing during the administration of rituximab.

Use of rituximab maybe associated with an increased risk of progressive multifocal leukoencephalopathy (PML). Patients must be monitored at regular intervals for any new or worsening neurological, cognitive or psychiatric symptoms that may be suggestive of PML. If

PML is suspected, further dosing must be suspended until PML has been excluded. If PML is confirmed the rituximab must be permanently discontinued.

The presence of a viral upper respiratory tract infection at the time of treatment may increase the risk of rituximab associated hepatotoxicity. Patients should be assessed for any cold or flu-like symptoms prior to treatment

Regimen

12 week cycle (starting 12 weeks after the last dose of induction chemotherapy) for 8 cycles

Drug	Dose	Days	Administration
Rituximab	1400mg	1	Subcutaneous injection over five minutes

Dose Information

- Subcutaneous rituximab should only be given to those who have had the intravenous formulation in the past.

Administration Information

Extravasation

- Rituximab SC – not applicable

Other

- Subcutaneous rituximab should be administered over approximately 5 minutes. The hypodermic injection needle must only be attached to the syringe immediately prior to administration to avoid potential needle clogging.

- Subcutaneous rituximab should be injected subcutaneously into the abdominal wall and never into areas where the skin is red, bruised, tender, hard or areas where there are moles or scars.

- During treatment with subcutaneous rituximab, other medicinal products for subcutaneous administration should preferably be given at different sites.

Additional Therapy

- Rituximab pre-medication

  15 -30 minutes prior to rituximab

  - Non-sedating oral antihistamine according to formulary choice
  - paracetamol 1000mg oral

- Rituximab infusion reactions

    - hydrocortisone 100mg intravenous bolus when required for rituximab infusion related reactions
    - salbutamol 2.5mg nebule when required for rituximab related bronchospasm
    - consider pethidine 25-50mg intravenous bolus for rituximab related rigors that fail to respond to steroids.

Coding

- Procurement – X71.3
- Delivery – X72.2

References
1. Salles G, Seymour JF, Offner F et al. Rituximab maintenance for 2 years in patients with high tumour burden follicular lymphoma responding to rituximab plus chemotherapy (PRIMA): a phase 3 randomised controlled trial. Lancet. 2011; 377(9759): 42-51.
2. Davies A, Merli F, Mihaljevic B et al. Pharmacokinetics and safety of subcutaneous rituximab in follicular lymphoma (SABRINA): stage 1 analysis of a randomised phase 3 study. Lancet Oncol. 2014 Mar;15(3):343-52

REGIMEN SUMMARY

Rituximab SC (12 weekly)

Day One

1. Antihistamine (non-sedating) oral
   Administration Instructions

   Non-sedating oral antihistamine according to local formulary choices. For example;
   - Cetirizine 10mg
   - Loratadine 10mg
   - Fexofenadine 120mg
   - Acrivastine 8mg

   Please record in journal or drug administration which antihistamine has been given

2. Paracetamol 1000mg oral

3. Rituximab 1400mg subcutaneous injection over five minutes into the abdominal wall

4. Hydrocortisone 100mg intravenous bolus once only when required for the relief of rituximab infusion related reactions

5. Salbutamol 2.5mg nebule once only when required for the relief of rituximab related bronchospasm

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	Sept 2014	None	Dr Debbie Wright Pharmacist	Dr Andrew Davies Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospital NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.