Systemic Anti-Cancer Therapy Protocol

Rituximab (Single Agent)

PROTOCOL REF: MPHARISAHA
(Version No: 1.0)

Approved for use in:

- CD20-positive indolent lymphoma or post-transplant lymphoproliferative disorder
- EBV reactivation after stem cell transplantation (NHSE Baseline Commissioning)
- Chronic graft versus host disease after stem cell transplantation (NHSE Baseline Commissioning)
- IGM related paraprotein nephropathy
- Rituximab naïve Waldenstrom's Macroglobulinaemia (NHSE Baseline Commissioning)

Blueteq registration is not required

Dosage:

Drug	Dose	Route	Frequency
Rituximab	**375mg/m^2**	IV infusion	Weekly for four weeks*

One cycle only

*A further 4 doses may be given every four weeks, or at weekly intervals, at the discretion of the clinician for the treatment of indolent lymphomas

Drug	Dose	Route	Frequency
Rituximab	**375mg/m^2**	IV infusion	Every four weeks

Four single dose cycles

Administration:

Due to the long retention time of rituximab in B cell depleted patients, women of childbearing potential should use effective contraceptive methods during and for 12 months following treatment with rituximab.

Anti-emetic risk:

Mildly emetogenic.

Supportive treatments:

Rituximab pre-infusion medicines:

- Paracetamol PO 1g
- Chlorphenamine IV bolus 10mg
- Hydrocortisone IV bolus 100mg

Supportive medicines:

- Allopurinol PO 100mg or 300mg OD (depending on renal function) for first cycle

Consider PCP prophylaxis if patient is being treated for post-transplant lymphoproliferative disorder or if another risk factor is present, e.g. immunosuppressive medication.

Extravasation risk:

Rituximab: non-vesicant

Refer to the Trust guidance for the prevention and management of extravasation

Interactions:

No significant interactions

Treatment schedule:

Weekly dosing

Day	Drug	Dose	Route	Diluent and rate
1	**Hydrocortisone sodium succinate**	**100mg**	**IV bolus**	Over 3-5 minutes
	Paracetamol	**1g**	**PO**	
	Chlorphenamine	**10mg**	**IV bolus**	Over 3-5 minutes
	Rituximab	**375mg/m^2**	**IV infusion**	In 500ml 0.9% NaCl. Infusion as per rituximab infusion rate policy.
8	**Hydrocortisone sodium succinate**	**100mg**	**IV bolus**	Over 3-5 minutes
	Paracetamol	**1g**	**PO**	
	Chlorphenamine	**10mg**	**IV bolus**	Over 3-5 minutes
	Rituximab	**375mg/m^2**	**IV infusion**	In 500ml 0.9% NaCl. Infusion as per rituximab infusion rate policy.
15	**Hydrocortisone sodium succinate**	**100mg**	**IV bolus**	Over 3-5 minutes
	Paracetamol	**1g**	**PO**	
	Chlorphenamine	**10mg**	**IV bolus**	Over 3-5 minutes
	Rituximab	**375mg/m^2**	**IV infusion**	In 500ml 0.9% NaCl. Infusion as per rituximab infusion rate policy.
22	**Hydrocortisone sodium succinate**	**100mg**	**IV bolus**	Over 3-5 minutes
	Paracetamol	**1g**	**PO**	
	Chlorphenamine	**10mg**	**IV bolus**	Over 3-5 minutes
	Rituximab	**375mg/m^2**	**IV infusion**	In 500ml 0.9% NaCl. Infusion as per rituximab infusion rate policy.

Monthly dosing:

Day	Drug	Dose	Route	Diluent and rate
1	**Hydrocortisone sodium succinate**	**100mg**	**IV bolus**	Over 3-5 minutes
	Paracetamol	**1g**	**PO**	
	Chlorphenamine	**10mg**	**IV bolus**	Over 3-5 minutes

	Rituximab	**375mg/m^2**	**IV infusion**	In 500ml 0.9% NaCl. Infusion as per rituximab infusion rate policy.

Main toxicities:

Severe cytokine release syndrome is characterised by severe dyspnoea, often accompanied by bronchospasm and hypoxia, in addition to fever, chills, rigors, urticaria, and angioedema.

Investigations and treatment plan:

	Pre	Prior to each cycle	Prior to each dose of rituximab	Ongoing
Informed Consent	X			
Clinical Assessment		X		
SACT Assessment (including performance status and toxicity assessment)			X	
FBC	X	X	X	
U&E & LFTs & Calcium profile	X	X	X	
CrCl (Cockcroft and Gault)	X			
CT scan and bone marrow biopsy	X			If clinically indicated
Blood pressure	X		X	Continuous monitoring required if on Rituximab
Temperature, respiratory rate, pulse			X	Continuous monitoring required if on Rituximab
Hepatitis B core antibody and surface antigens & Hep C & HIV 1+2	X			
Height	X			
Weight	X	X		
Pregnancy test	X			Where appropriate

Dose Modifications and Toxicity Management:

Severe infusion-related reactions with fatal outcome can have an onset ranging within 30 minutes to 2 hours after starting the first rituximab infusion. They can be characterized by pulmonary events and in some cases included rapid tumour lysis and features of tumour lysis syndrome (TLS) in addition to fever, chills, rigors, hypotension, urticaria, and angioedema.

Severe cytokine release syndrome may occur. Monitor patients closely. Patients who develop evidence of severe reactions, especially severe dyspnea, bronchospasm or hypoxia should have infusion interrupted immediately. The patient should then be evaluated for evidence of TLS including appropriate laboratory tests and, for pulmonary infiltration, with a chest x-ray. The infusion should not be restarted until complete resolution of all symptoms, and normalisation of laboratory values and chest x-ray findings. At this time, the infusion can be initially resumed at not more than one-half the previous rate. If the same adverse reaction occurs for a second time, the decision to stop the treatment should be seriously considered on a case-by-case basis.

Anaphylactic and other hypersensitivity reactions may occur. In contrast to cytokine release syndrome, true hypersensitivity reactions typically occur within minutes after starting infusion.

Mild or moderate infusion-related reactions usually respond to a reduction in the rate of infusion. The infusion rate may be increased upon improvement of symptoms

References:

1. https://www.medicines.org.uk/emc rituximab (accessed 05/2020)

2. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20: e201–08.

3. McLaughlin P, Grillo-López AJ, Link BK, Levy R, Czuczman MS, Williams ME, Heyman MR, BenceBruckler I, White CA, Cabanillas F, Jain V, Ho AD, Lister J, Wey K, Shen D, Dallaire BK. Rituximab chimeric anti-CD20 monoclonal antibody therapy for relapsed indolent lymphoma: half of patients respond to a four-dose treatment program. J Clin Oncol. 1998 Aug;16(8):2825-33.

4. Trappe et al. Sequential treatment with rituximab followed by CHOP chemotherapy in adult B-cell posttransplant lymphoproliferative disorder (PTLD): the prospective international multicentre phase 2 PTLD-1 trial. Lancet oncol. 2012; 13 (2) 196-206

5. Trappe et al. Response to Rituximab Induction Is a Predictive Marker in B-Cell Post-Transplant Lymphoproliferative Disorder and Allows Successful Stratification Into Rituximab or R-CHOP Consolidation in an International, Prospective, Multicenter Phase II Trial J Clin Oncol. 2017 Feb 10;35(5):536-543.